Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Table of Contents

Guidelines Development Process

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the Guidelines	Provide guidance to HIV care practitioners in the United States on the optimal use of antiretroviral (ARV) agents to treat HIV infection in pregnant women and to prevent perinatal HIV transmission in HIV-exposed infants.
Panel Members	The Panel is composed of approximately 30 voting members who have expertise in managing the care of pregnant women with HIV (e.g., training in obstetrics/gynecology, infectious diseases, or women's health), pharmacology of ARV drugs during pregnancy, and interventions for prevention of perinatal transmission (e.g., specialized training in pediatric HIV infection). The Panel also includes community representatives with knowledge of HIV infection in pregnant women and interventions for prevention of perinatal transmission. The U.S. government representatives, appointed by their agencies, include at least one representative from each of the following Department of Health and Human Services agencies: the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration (HRSA), and the National Institutes of Health (NIH). Members who do not represent U.S. government agencies are selected by Panel members after an open call for nominations. Each member serves on the Panel for a 3-year period, with an option for re-appointment. The Panel may also include liaison members from the National Perinatal HIV Hotline, the American Academy of Pediatrics' Committee on Pediatric AIDS, and the American College of Obstetricians and Gynecologists. A list of all Panel members can be found in the Guidelines Panel Members section.
Financial Disclosures	All members of the Panel submit an annual written financial disclosure that reports any association with manufacturers of ARV drugs or diagnostics used to manage HIV infection. See Financial Disclosure for a list of the latest disclosures.
Users of the Guidelines	Providers of care to pregnant women with HIV and to infants who have been exposed to HIV
Developer	The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding Source	Office of AIDS Research, NIH
Evidence for Recommendations	The recommendations in these guidelines are generally based on studies published in peer-reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data that was presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation Grading	See Table 2.
Method of Synthesizing Data	Each section of the guidelines is assigned to a small group of Panel members with expertise in the area of interest. A structured literature search is conducted by a technical assistance consultant and provided to the Panel working group. The members review and synthesize the available data and propose recommendations to the entire Panel. The Panel discusses all proposals during monthly teleconferences. Proposals are modified based on Panel discussions and then distributed, with ballots, to all Panel members. If there are substantive comments or votes against approval, the recommended changes and areas of disagreement are brought back to the full Panel (via email or teleconference) for review, discussion, and further modification to reach a final version that is acceptable to all Panel members. The recommendations in these final versions represent consensus of Panel members and are included in the guidelines as official Panel recommendations.
Other Guidelines	These guidelines focus on pregnant women with HIV and their infants. Other guidelines (all of which are available on the AIDS*info* website) outline the use of ARV agents in nonpregnant adults and adolescents with HIV; use of ARV agents in infants and children with HIV; treatment and prevention of opportunistic infections (OIs) in adults and adolescents with HIV, including pregnant women; treatment and prevention of OIs in children who have been exposed to HIV or who have HIV infection; and treatment of people who experience occupational or nonoccupational exposure to HIV. Preconception management for nonpregnant women of reproductive potential is briefly discussed in this document. However, for a more detailed discussion of the issues surrounding the treatment of nonpregnant adults, please consult the Adult and Adolescent Antiretroviral Guidelines and the Adult and Adolescent Opportunistic Infection Guidelines.

Guidelines Development Process

Table 1. Outline of the Guidelines Development Process, cont'd

Topic	Comment
Update Plan	The Panel meets monthly by teleconference to review data that may affect the content of the guidelines. Updates may be prompted by new drug approvals (or new indications, new dosing formulations, and/or changes in dosing frequency), significant new safety or efficacy data, or other information that may have a significant impact on the clinical care of patients. In the event of significant new data that may affect patient safety, the Panel may issue a warning announcement and recommendations on the AIDS*info* website until the guidelines can be updated with appropriate changes.
Public Comments	A 2-week public comment period follows the release of the updated guidelines on the AIDS*info* website. The Panel reviews comments to determine whether additional revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at contactus@aidsinfo.nih.gov.

Table 2. Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement **B:** Moderate recommendation for the statement **C:** Optional recommendation for the statement	**I:** One or more randomized trials with clinical outcomes and/or validated laboratory endpoints **II:** One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes **III:** Expert opinion

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 1 of 8)

Note: All recommendations in the following table are based on consensus expert opinion. More details can be found in the CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2016.

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs							
EFV	**COC:** • No effect on EE concentrations • ↓ active metabolites of norgestimate; LN AUC ↓ 83% and norelgestromin AUC ↓ 64%[35] • Etonogestrel (in COC) C_{24h} ↓ 61%[41] **DMPA:** • No effect on DMPA levels[32,34] **Etonogestrel Implant:** • Etonogestrel AUC ↓ 63% to 82%[51,53] **LN Implant:** • LN AUC ↓ 47%[46] • LN (emergency contraception) AUC ↓ 58%[30] **Changes in ARV Levels and/or Effects on HIV** *COC:* • No effect on EFV concentrations[35] • EFV C_{12h} ↓ 22%; was under therapeutic threshold in three of 16 subjects[41] *DMPA:* • No effect on HIV disease progression[32,54,55] • No effect on EFV concentrations[32] **LN Implant:** • No effect on HIV disease progression[46] **Vaginally Administered Etonogestrel/EE:** • Etonogestrel ↓ 79% • EE ↓ 59%	**COC:** • No difference in pregnancy rates[52] • Pregnancy rate was 13% higher in women using COCs and EFV than in women using COCs alone[50,56] • Progesterone >3 ng/mL (a surrogate for ovulation) in three of 16 women[57] • No ovulations[35] **DMPA:** • No increase in pregnancy rates[32,50,52,55] • Low progesterone[32,34,55] **Etonogestrel Implant:** • Pregnancy rate higher with EFV compared with no ART, but still lower with implants than with other hormonal methods of contraception[50] • Presumptive ovulation in 5%[53] **LN Implant:** • 12% pregnancy rate[42] • 15% pregnancy rate[46] • Pregnancy rate higher with EFV compared with no ART, but still lower with implants than with other hormonal methods of contraception[50] • No increase in pregnancy rate[52]	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, some studies suggest higher pregnancy rate and ovulation rate and decreased progestin levels. EFV may decrease, but clinical significance unclear. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. Also, no effect on HIV disease progression or EFV levels. For implants, some studies suggest higher pregnancy rate and decreased hormone levels. For vaginally administered etonogestrel/EE, PK evaluation showed that etonogestrel levels were 79% lower and EE levels were 59% lower in participants on EFV than in controls after 21 days.[58]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 2 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
ETR	EE AUC ↑ 22%[59] No significant effect on NE[59]	**COC:** • No ovulations[59]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, one study found no ovulations and no significant change in progestin levels. No data on POPs.
NVP	EE AUC ↓ 29%;[60] no change in EE AUC[61] NE AUC ↓ 18%[60] Etonogestrel (in COC) C_{24h} ↓ 22%[41] **DMPA:** • No significant change[32] **LN Implant:** • LN AUC ↑ 35%[46] **Changes in ARV Levels and/or Effects on HIV** *COC:* • No significant effect on NVP levels[57,60,62] *DMPA:* • No effect on HIV disease progression[32,54,55,63] *LN Implant:* • No effect on HIV disease progression[46,64]	**COC:** • No increase in pregnancy rate[50,52,56,65,66] • No ovulations[57,61,66] **DMPA:** • No increase in pregnancy rate[50,52,55,65] • No ovulations[32] **Etonogestrel Implant:** • No increase in pregnancy rate[50] **LN Implant:** • No increase in pregnancy rate[42,46,50,52,64]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed	For COCs, evidence does not show effects on pregnancy rate or ovulations. Evidence demonstrated small decrease in progestin levels. No effect on NVP levels. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. No effect on HIV disease progression. For implants, evidence does not show effects on pregnancy rate or HIV disease progression.
RPV	EE AUC ↑ 14%[40] No significant change on NE.[40] **Changes in ARV Levels and/or Effects on HIV** *COC:* • No change in RPV levels compared to historical controls[40]	**COC:** • No change in progesterone[40]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, evidence does not show effects on ovulation or progestin levels. No change in RPV levels. No data on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 3 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
DOR	No clinically significant interaction with EE and LN	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No clinical data.
RTV-Boosted PIs							
ATV/r	EE AUC ↓ 19%[67] Norgestimate AUC ↑ 85%[67] **POP:** • NE AUC ↑ 50%[68] **Vaginally Administered Etonogestrel/EE:** • Etonogestrel ↑ 71% • EE ↓ 38%[58]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, increase in progestin levels seen in only one study. For POPs, increase in progestin levels seen in only one study. RTV inhibits CYP3A4, which may increase contraceptive hormone levels.
DRV/r	EE AUC ↓ 44%[69] NE AUC ↓ 14%[69]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, small decrease in progestin levels. No data on POPs.
FPV/r	EE AUC ↓ 37%[70] NE AUC ↓ 34%[70] No change in FPV/r levels[70]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, decrease in progestin levels. No data on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 4 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
LPV/r	EE AUC ↓ 55%[31] NE AUC ↓ 17% **Patch:** • EE AUC ↓ 45%[31] • Norelgestromin AUC ↑ 83%[31] **DMPA:** • DMPA AUC ↑ 46%[44] **Etonogestrel Implant:** • Etonogestrel AUC ↑ 52%[53] **Changes in ARV Levels and/or Effects on HIV** *Patch:* • LPV/r ↓ 19%[31] *DMPA:* • No effect on HIV disease progression[44] • No change in LPV/r levels[44]	**COC:** • Increased pregnancy rate, but CIs overlap[50] **Patch:** • No ovulations[31] **DMPA:** • No pregnancies and no ovulations[44] • Increased pregnancy rate, but CIs overlap[50] **Etonogestrel Implant:** • No increase in pregnancy rate[50] **LN Implant:** • No increase in pregnancy rate[42,50]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, nonsignificant increase in pregnancy rate. Small decrease in progestin level. For patch, no ovulations and progestin levels increased. For DMPA, evidence shows no effect on pregnancy rate or ovulations. Progestin levels increased. For implants, evidence shows no effect on pregnancy rate. Progestin levels increased.
SQV/r	↓ EE[71] **Changes in ARV Levels and/or Effects on HIV** *COC:* • No change in SQV/r levels[72]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No information on progestin levels for CHCs or POPs. RTV inhibits CYP3A4, which may increase contraceptive hormone levels. However, some PI/r cause decreases in progestin levels, so there are theoretical concerns about contraceptive effectiveness.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 5 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
TPV/r	EE AUC ↓ 48%[73] No significant change on NE.[73] **Changes in ARV Levels and/or Effects on HIV:** • No change in TPV levels[73]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, no significant change in progestin levels, but the only data available are from the product label. No data on POPs. RTV inhibits CYP3A4, which may increase contraceptive hormone levels. However, some PI/r cause decreases in progestin levels, so there are theoretical concerns about contraceptive effectiveness.
COBI-Boosted PIs							
ATV/c	Drospirenone AUC ↑ 2.3-fold EE AUC ↓ 22%[74]	N/A	**Contraindicated** with drospirenone-containing hormonal contraceptives due to potential for hyperkalemia. Consider alternative or additional contraceptive method.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No data on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 6 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
COBI-Boosted PIs, continued							
DRV/c	Drospirenone AUC ↑ 1.6-fold EE AUC ↓ 30%[74]	N/A	Clinical monitoring is recommended when DRV/c is used in combination with drospirenone-containing COCs, due to the potential for hyperkalemia. Consider alternative or additional contraceptive method.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No data on POPs.
PIs without RTV							
ATV	**COC:** • EE AUC ↑ 48%[75] • NE AUC ↑ 110%[75]	N/A	Prescribe oral contraceptive that contains no more than 30 mcg of EE or recommend alternative contraceptive method.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, increased concentrations of estrogen and progestin, but the only data available are from the product label. No data on POPs.
FPV	**COC** *APV:* • No change in EE AUC; C_{min} ↑ 32% • NE AUC ↑ 18%; C_{min} ↑ 45%[70] **FPV with EE/NE:** • APV AUC ↓ 22%; C_{min} ↓ 20%[70]	N/A	Use alternative contraceptive method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Use of FPV alone with EE/NE may lead to loss of virologic response. No data on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 7 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
PIs without RTV, continued							
IDV	**COC:** • EE AUC ↑ 22% • NE AUC ↑ 26%[76]	**COC:** • No pregnancies among women taking IDV and COCs[56]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, small increases in EE and progestin have been observed, and one clinical study did not suggest any efficacy concerns. No data on POPs.
NFV	**COC:** • EE AUC ↓ 47% • NE AUC ↓ 18%[77] **DMPA:** • No change[32] **NFV:** • AUC ↓ 18%	**COC:** • One small study suggested that women using COCs and NFV may have had higher pregnancy rates than those using COCs alone.[56] **DMPA:** • No pregnancies and no ovulations[32,55] • No change in CD4 count or HIV RNA[32,55]	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, a small decrease in progestin and a decrease in estrogen have been observed; one small clinical study suggested possible higher pregnancy rate with COC and NFV use. For DMPA, PK and clinical data demonstrate no change. However, NFV AUC slightly decreased. No data on POPs or implants.
CCR5 Antagonist							
MVC	**COC:** • No significant effect on EE or LN[78]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, no change in EE or progestin. No clinical data. No data on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 8 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
INSTIs							
BIC/FTC/ TAF	No significant drug interactions with EE or norgestimate.	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No clinical data.
DTG	**COC:** • No significant effect on norgestimate or EE • No change in DTG AUC[45]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, no change in EE or progestin. No clinical data. No data on POPs.
EVG/c	**COC:** • Norgestimate AUC ↑ 126% EE AUC ↓ 25%[79]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	When administered as the four-drug regimen EVG/c/FTC/TDF, increases in progestin and a small decrease in EE were observed. No clinical data. No data on POPs.
RAL	**COC:** • No change in EE • Norgestimate AUC ↑ 14%[80]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, no change in EE and a small increase in progestin. No clinical data. No data on POPs.

[a] Because the hormonal levels achieved with DMPA are substantially higher than the levels that are required for contraception, any small reduction in hormonal level due to ARV drugs is unlikely to reduce contraceptive effectiveness.

Key to Symbols: ↑ = increase ↓ = decrease

Key: APV = amprenavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{12h} = concentration at 12 hours post-dose; C_{24h} = concentration at 24 hours post-dose; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; CHC = combination hormonal contraceptives; CI = confidence interval; C_{min} = minimum plasma concentration; COBI = cobicistat; COC/P/R = combined oral contraceptives/patch/ring; CYP = cytochrome P450; DMPA = depot medroxyprogesterone acetate; DOR= doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EE = ethinyl estradiol; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LN = levonorgestrel; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NE = norethindrone; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; P = progestin; PI = protease inhibitor; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; POP = progesterone-only oral contraceptive pills; RPV = rilpivirine; RTV = ritonavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Tables 21a, 21b, and 21d.

Table 4. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (Last updated December 12, 2019; last reviewed: December 12. 2019) (page 1 of 4)

Recommendations for initial therapy are intended for pregnant women **who have never received ART or ARV drugs for prophylaxis** (i.e., women who are ARV-naive) and who have no evidence of significant resistance to regimen components (also see Pregnant Women Living with HIV Who Have Never Received Antiretroviral Drugs and Table 5).

In general, the Panel recommends that **women who are already on fully suppressive ART regimens when pregnancy occurs should continue to use those regimens**, unless they are receiving an ARV drug or ART regimen that is not recommended for use in adults or there are concerns about safety and inferior efficacy during pregnancy (see Table 5 and Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy). Clinicians may need to consider additional factors when initiating ART in women who previously received ART or ARV drugs for prophylaxis (see Pregnant Women Living with HIV Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications and Table 5).

Regimens are listed alphabetically within each drug class and recommendation category, and the order does not indicate a ranking of preference. In addition, the Panel makes no recommendation of one agent or regimen over another within each category (*Preferred* or *Alternative*).

Note: For more information about the use of specific drugs and dosing in pregnancy, see Table 5, the individual drug sections in Appendix B, and Table 8.

Drug or Drug Combination	Comments
Preferred Initial Regimens in Pregnancy Drugs or drug combinations are designated as *Preferred* for therapy in pregnant women when clinical trial data in adults have demonstrated efficacy and durability with acceptable toxicity and ease of use, and pregnancy-specific PK data are available to guide dosing. In addition, the available data must suggest a favorable risk-benefit balance for the drug or drug combination compared to other ARV drug options; the assessment of risks and benefits should incorporate outcomes for women, fetuses, and infants. Some *Preferred* drugs or regimens may have minimal toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive. Therefore, it is important to read all the information on each drug in the Perinatal Guidelines before administering any of these medications to patients (also see Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy).	
Preferred Dual-NRTI Backbones	
ABC/3TC	Available as an FDC. Can be administered once daily. ABC **should not be used** in patients who test positive for HLA-B*5701 because of the risk of developing a hypersensitivity reaction. ABC/3TC administered with ATV/r or EFV is not recommended if pretreatment HIV RNA is >100,000 copies/mL.
TDF/FTC ***or*** **TDF/3TC**	TDF/FTC is available as an FDC. Either coformulated TDF/FTC or separate doses of TDF and 3TC can be administered once daily. TDF has potential renal toxicity; thus, TDF-based, dual-NRTI combinations should be used with caution in patients with renal insufficiency.
Preferred INSTI Regimens	
DTG/ABC/3TC (FDC) ***or*** **DTG plus a Preferred Dual-NRTI Backbone**[a]	Administered once daily. The use of DTG/ABC/3TC requires HLA-B*5701 testing, because this FDC contains ABC. INSTI-based regimens may be useful when drug interactions or the potential for preterm delivery with a PI-based regimen are a concern. In nonpregnant adults, DTG is associated with lower rates of INSTI resistance than RAL; like RAL, DTG has been shown to rapidly decrease viral load in ARV-naive pregnant women who present to care later in pregnancy. DTG is *Preferred* for the treatment of pregnant women with acute HIV infection and for women who present to care late in pregnancy. There are specific timing and/or fasting recommendations if DTG is taken with calcium or iron (e.g., in prenatal vitamins; see Table 8). The use of DTG at conception and in very early pregnancy has been associated with a small but statistically significant increase in the risk of NTDs; this information should be discussed with patients to ensure informed decision-making. For more information, see Updated Guidance About the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 5, Teratogenicity, and Appendix D: Dolutegravir Counseling Guide for Health Care Providers.

Table 4. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 2 of 4)

Drug or Drug Combination	Comments
RAL plus a Preferred Dual-NRTI Backbone	PK data are available for RAL use in pregnancy, and experience with use in pregnancy is increasing. RAL has been shown to produce rapid viral load decline to undetectable levels in women who present for initial therapy late in pregnancy. INSTI-based regimens may be useful when drug interactions or the potential for preterm delivery with PI-based regimens are a concern. Twice-daily dosing required. There are specific timing and/or fasting recommendations if RAL is taken with calcium or iron (e.g., in prenatal vitamins; see Table 8).
Preferred PI Regimens	
ATV/r plus a Preferred Dual-NRTI Backbone	Once-daily administration. Extensive experience with use in pregnancy. Maternal hyperbilirubinemia; no clinically significant neonatal hyperbilirubinemia or kernicterus reported, but neonatal bilirubin monitoring is recommended. Cannot be administered with PPIs. Specific timing recommended for dosing with H2 blockers (see Table 8).
DRV/r plus a Preferred Dual-NRTI Backbone	Better tolerated than LPV/r. Experience with use in pregnancy is increasing. Must be used twice daily in pregnancy.
Drug	**Comments**
Alternative Initial Regimens in Pregnancy Drugs or drug combinations are designated as *Alternative* options for therapy in pregnant women when clinical trial data in adults show efficacy and the data in pregnant individuals are generally favorable but limited. Most *Alternative* drugs or regimens are associated with more PK, dosing, tolerability, formulation, administration, or interaction concerns than those in the *Preferred* category, but they are acceptable for use in pregnancy. Some *Alternative* drugs or regimens may have known toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive. Therefore, it is important to read all the information on each drug in the Perinatal Guidelines before administering any of these medications to patients (also see Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy).	
Alternative Dual-NRTI Backbones	
ZDV/3TC	Available as an FDC. Although not recommended for initial therapy in nonpregnant adults, ZDV/3TC is the NRTI combination with most experience for use in pregnancy. It has the disadvantages of requiring twice-daily administration and having an increased potential for hematologic toxicities and other toxicities.
Alternative PI Regimens	
LPV/r plus a Preferred Dual-NRTI Backbone	Abundant experience and established PKs in pregnancy. More nausea than with *Preferred* agents. Twice-daily administration. A dose increase is recommended during the third trimester (see Table 8). Once-daily LPV/r **is not recommended** for use in pregnant women.
Alternative NNRTI Regimens	
EFV/TDF/FTC (FDC) ***or*** **EFV/TDF/3TC (FDC)** ***or*** **EFV plus a Preferred Dual-NRTI Backbone**	Birth defects have been reported in primate studies of EFV, but there has been no evidence of an increased risk of birth defects in human studies and extensive experience in pregnancy; cautionary text remains in package insert (see Teratogenicity and Table 8). These regimens are useful for women who require treatment with drugs that have significant interactions with *Preferred* agents, or who need the convenience of a coformulated, single-tablet, once-daily regimen and are not eligible for DTG or RPV. Screening for antenatal and postpartum depression is recommended. Higher rate of adverse events than some *Preferred* drugs.
RPV/TDF/FTC (FDC) ***or*** **RPV plus a Preferred Dual-NRTI Backbone**	RPV **is not recommended** in patients with pretreatment HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm^3. Do not use with PPIs. PK data are available for pregnant individuals, but there is relatively little experience with use in pregnancy. PK data suggest lower drug levels and risk of viral rebound in second and third trimesters; if used, consider monitoring viral load more frequently. Should be taken with food. Available in a coformulated, single-tablet, once-daily regimen.
Drug	**Comments**
Insufficient Data in Pregnancy to Recommend for Initial Regimens in ART-Naive Women These drugs are approved for use in adults but lack adequate pregnancy-specific PK or safety data.	
BIC/TAF/FTC (FDC)	No data on the use of BIC in pregnancy. Limited data on the use of TAF in pregnancy.

Table 4. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 3 of 4)

Drug	Comments
DOR	No data on the use of DOR in pregnancy.
IBA	No data on the use of IBA in pregnancy.
TAF/FTC (FDC) ***or*** **RPV/TAF/FTC (FDC)**	Plasma TAF exposures in pregnant adults are similar to those seen in nonpregnant adults, whether TAF is administered with a boosting agent or not. TAF has been studied in pregnant women, but data are not yet sufficient to recommend initiating TAF in pregnancy.
Drug	**Comments**
Not Recommended for Initial ART or Use in Pregnancy These drugs and drug combinations are recommended for use in adults but **are not recommended** for use during pregnancy because of concerns about maternal or fetal safety or inferior efficacy, including viral breakthroughs in the second and third trimester (see Table 5 and Table 8). **Note:** When a pregnant woman presents to care while virally suppressed on one of these drugs or drug combinations, providers should consider whether to continue her current regimen or switch to a recommended ART regimen (see Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy and Table 5).	
ATV/c	Limited data on the use of ATV with COBI in pregnancy. Substantial reductions in trough levels of ATV in the second and third trimesters have been reported when taken with COBI.
DRV/c (FDC) ***or*** **DRV/c/FTC/TAF (FDC)**	Limited data on use of DRV with COBI in pregnancy. Inadequate levels of both DRV and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Insufficient data about the use of TAF in pregnancy (see above).
EVG/c/FTC/TAF (FDC)	Limited data on use of EVG with COBI and insufficient data on the use of TAF in pregnancy (see above). Inadequate levels of both EVG and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Specific timing and/or fasting recommendations, especially if taken with calcium or iron (e.g., in prenatal vitamins; see Table 8).
EVG/c/FTC/TDF (FDC)	Limited data on use of EVG with COBI in pregnancy. Inadequate levels of both EVG and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Specific timing and/or fasting recommendations, especially if taken with calcium or iron (e.g., in prenatal vitamins; see Table 8).
Drug	**Comments**
Not Recommended for Initial ART in Pregnancy and Not Recommended Except in Special Circumstances for Treatment-Experienced Women in Pregnancy These drugs **are not recommended** for use in pregnant women who have never received ART. With the exception of NVP, data about the PKs, safety, and efficacy of these drugs during pregnancy are limited. Some of these drugs are also categorized as not recommended except in special circumstances during pregnancy, because the Panel recognizes that there may be circumstances where pregnant women who are ART-experienced may need to initiate or continue these drugs to reach or maintain viral suppression (see Table 5).	
ETR	Not recommended for use in ART-naive populations. Available PK data suggest that using the standard adult dose is appropriate for pregnant patients, although data about use in pregnancy are limited.
MVC	Not recommended for use in ART-naive populations. MVC requires tropism testing before use. Available PK data suggest that using the standard adult dose is appropriate for pregnant patients, although data about use in pregnancy are limited.
NVP	Not recommended because of the potential for adverse events, complex lead-in dosing, and low barrier to resistance. NVP should be used with caution when initiating ART in women with CD4 counts >250 cells/mm^3. Use NVP and ABC together with caution; both can cause hypersensitivity reactions in the first few weeks after initiation.
T-20	Not recommended for use in ART-naive populations.

Table 4. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 4 of 4)

[a] The decision to designate DTG as a *Preferred* ARV drug for therapy in pregnant women, irrespective of trimester, was based on several factors. First, DTG is associated with higher rates of virologic suppression, faster rates of viral load decline, and a higher genetic barrier to drug resistance than other *Preferred* and *Alternative* agents. Second, a recent study that evaluated a large number of pregnancies has shown that the risk of NTDs is lower than previously reported in preliminary data. This risk is also largely limited to a short period of time (before 6 weeks post-last menstrual period). A very small minority of women with HIV initiate their first ART regimen during this period of time. Some Panel members would avoid using DTG in women who are initiating ART before 6 weeks gestation. After this time, any additional risk of NTDs due to DTG is minimal. Third, data are extremely limited on the risks that are associated with using other *Preferred* and *Alternative* ARV drugs preconception or in very early pregnancy; this lack of data does not indicate either the presence or absence of risk when using alternatives to DTG. DTG is recommended as an *Alternative* agent for people who are trying to conceive, as these patients have more time to achieve virologic suppression on regimens that do not contain DTG. For additional information, see Teratogenicity, Updated Guidance About the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs in Pregnancy, and Appendix D: Dolutegravir Counseling Guide for Health Care Providers.

Note: The following drugs and drug combinations (that are not listed above) should not be used during pregnancy; if women become pregnant while taking these medications, they should switch to a recommended regimen: d4T, ddI, FPV, FPV/r, IDV, IDV/r, NFV, RTV (as the sole PI), SQV, SQV/r, TPV, TPV/r, two-drug ART regimens, or a three-NRTI ART regimen (e.g., ABC/ZDV/3TC). See Archived Drugs in the Perinatal Guidelines and What Not to Use in the Adult and Adolescent Antiretroviral Guidelines for individual ARV drugs, ARV combinations, and ART regimens that are not recommended or that should not be used in adults.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CD4 = CD4 T lymphocyte cell; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IBA = ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; NVP = nevirapine; the Panel = the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 5. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (Last updated December 12, 2019; last reviewed December 12, 2019) (page 1 of 4)

Women should be given information about the benefits and risks of initiating an ARV regimen or making changes to an existing regimen so they can make informed decisions about their care. Patient autonomy and informed choice should be considered in all aspects of medical care, including HIV and obstetric care. This is the primary guiding principle in all the Panel's recommendations.

ART Regimen Component	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[a]	New ARV Regimen for Pregnant Women Whose Current Regimen is Not Well Tolerated and/or is Not Fully Suppressive[a]	ART for Nonpregnant Women Who Are Trying to Conceive[a,b]
INSTIs Used in combination with a dual-NRTI backbone[c]					
DTG[d]	Preferred	Continue	Preferred	Preferred	Alternative
RAL	Preferred	Continue	Preferred	Preferred	Preferred
BIC	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
EVG/c[e]	Not recommended	Consider switching, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
PIs Used in combination with a dual-NRTI backbone[c]					
ATV/r	Preferred	Continue	Preferred	Preferred	Preferred
DRV/r	Preferred	Continue	Preferred	Preferred	Preferred
LPV/r	Alternative	Continue	Alternative	Alternative	Alternative
ATV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
DRV/c[e]	Not recommended	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring	Not recommended	Not recommended	Not recommended
NNRTIs Used in combination with a dual-NRTI backbone[c]					
EFV	Alternative	Continue	Alternative	Alternative	Alternative
RPV[f]	Alternative	Continue	Alternative	Alternative	Alternative
DOR	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
ETR[g]	Not recommended	Continue	Not recommended, except in special circumstances	Not recommended, except in special circumstances	Not recommended, except in special circumstances

Table 5. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (page 2 of 4)

ART Regimen Component	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[a]	New ARV Regimen for Pregnant Women Whose Current Regimen is Not Well Tolerated and/or is Not Fully Suppressive[a]	ART for Nonpregnant Women Who Are Trying to Conceive[a,b]
NNRTIs Used in combination with a dual-NRTI backbone[c]					
NVP[g]	Not recommended	Continue	Not recommended, except in special circumstances	Not recommended, except in special circumstances	Not recommended, except in special circumstances
NRTIs[c,h]					
ABC[i]	Preferred	Continue	Preferred	Preferred	Preferred
FTC	Preferred	Continue	Preferred	Preferred	Preferred
3TC	Preferred	Continue	Preferred	Preferred	Preferred
TDF	Preferred	Continue	Preferred	Preferred	Preferred
ZDV	Alternative	Continue	Alternative	Alternative	Alternative
TAF[j]	Insufficient data	Continue	Insufficient data	Insufficient data	Insufficient data
Entry and Fusion Inhibitors					
IBA	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
MVC[g]	Not recommended	Continue	Not recommended, except in special circumstances	Not recommended, except in special circumstances	Not recommended, except in special circumstances
T-20[g]	Not recommended	Continue	Not recommended, except in special circumstances	Not recommended, except in special circumstances	Not recommended, except in special circumstances
FDC Regimens[e,h] The individual drug component that is most responsible for the overall recommendation is indicated in parentheses.					
ABC/DTG/3TC[d,i]	Preferred	Continue	Preferred	Preferred	Alternative (DTG)
EFV/FTC/TDF	Alternative (EFV)	Continue	Alternative (EFV)	Alternative (EFV)	Alternative (EFV)
EFV/3TC/TDF	Alternative (EFV)	Continue	Alternative (EFV)	Alternative (EFV)	Alternative (EFV)
FTC/RPV/TDF[f]	Alternative (RPV)	Continue (RPV)	Alternative (RPV)	Alternative (RPV)	Alternative (RPV)
BIC/FTC/TAF	Insufficient data (BIC, TAF)	Insufficient data (BIC)	Insufficient data (BIC, TAF)	Insufficient data (BIC, TAF)	Insufficient data (BIC, TAF)
DOR/3TC/TDF	Insufficient data (DOR)	Insufficient data (DOR)	Insufficient data (DOR)	Insufficient data (DOR)	Insufficient data (DOR)

Table 5. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (page 3 of 4)

ART Regimen Component	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[a]	New ARV Regimen for Pregnant Women Whose Current Regimen is Not Well Tolerated and/or is Not Fully Suppressive[a]	ART for Nonpregnant Women Who Are Trying to Conceive[a,b]
FDC Regimens[e,h] The individual drug component that is most responsible for the overall recommendation is indicated in parentheses.					
FTC/RPV/TAF	Insufficient data (TAF[i])	Continue (RPV[f], TAF[i]) or consider switching to FTC/RPV/TDF	Insufficient data (TAF[i])	Insufficient data (TAF[i])	Insufficient data (TAF[i])
EVG/c/FTC/TDF[e]	Not recommended (EVG/c)	Consider switching, or continuing the same regimen with frequent viral load monitoring (EVG/c)	Not recommended (EVG/c)	Not recommended (EVG/c)	Not recommended (EVG/c)
EVG/c/FTC/TAF[e]	Not recommended (EVG/c)	Consider switching, or continuing the same regimen with frequent viral load monitoring (EVG/c)	Not recommended (EVG/c)	Not recommended (EVG/c)	Not recommended (EVG/c)
DRV/c/FTC/TAF[e]	Not recommended (DRV/c)	Consider switching, or continuing the same regimen with frequent viral load monitoring (DRV/c)	Not recommended (DRV/c)	Not recommended (DRV/c)	Not recommended (DRV/c)
DTG/3TC As a complete regimen[k]	Not recommended	Not recommended; switch, or add additional agents	Not recommended	Not recommended	Not recommended
DTG/RPV As a complete regimen[k]	Not recommended	Not recommended; switch, or add additional agents[f]	Not recommended	Not recommended	Not recommended

[a] **Do not initiate** ARV regimens with components that have documented resistance or suspected resistance based on prior ARV exposure.

[b] This guidance is intended for women who are trying to conceive. These recommendations are not intended for all women with HIV who might become pregnant.

[c] ABC plus 3TC, TDF plus FTC, and TDF plus 3TC are *Preferred* dual-NRTI backbones, and ZDV plus 3TC is an *Alternative* dual-NRTI backbone for ARV regimens.

[d] The decision to designate DTG as a *Preferred* ARV drug for therapy in pregnant women, irrespective of trimester, was based on several factors. First, DTG is associated with higher rates of virologic suppression, faster rates of viral load decline, and a higher genetic barrier to drug resistance than other *Preferred* and *Alternative* agents. Second, a recent study that evaluated a large number of pregnancies has shown that the risk of NTDs is lower than previously reported in preliminary data. This risk is also largely limited to a short period of time (before 6 weeks post-last menstrual period). A very small minority of women with HIV initiate their first ARV regimen during this period of time. Some Panel members would avoid using DTG in women who are initiating ART before 6 weeks of gestation. After this time, any additional risk of NTDs due to DTG is minimal. Third, data are extremely limited on the risks that are associated with using other *Preferred* and *Alternative* ARV drugs preconception or in very early pregnancy; this lack of data does not indicate either the presence or absence of risk when using alternatives to DTG. DTG is recommended as an Alternative agent for people trying to conceive, as these patients have more time to achieve virologic suppression on regimens that do not contain DTG. For additional information see Teratogenicity, Updated Guidance About the Use of Dolutegravir in Pregnancy in Recommendations for the Use of Antiretroviral Drugs in Pregnancy, and Appendix D: Dolutegravir Counseling Guide for Health Care Providers.

Table 5. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (page 4 of 4)

[e] DRV/c, EVG/c, and ATV/c **are not recommended** for use in pregnancy due to PK changes that pose a risk for low drug levels and viral rebound in the second and third trimesters. However, in cases where virologically suppressed pregnant women present to care on regimens that include these drugs, clinicians can consider continuing the use of these drug combinations with frequent viral load monitoring. If there are concerns about switching, see Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy.

[f] Although PK data indicate that RPV plasma concentration is reduced during the second and third trimester, the reduction is less than the reductions seen with use of EVG/c or DRV/c. Higher-than-standard doses of RPV have not been studied, so there are insufficient data to recommend a dose change in pregnancy. With standard dosing, viral load should be monitored more frequently.

[g] Although these drugs are not recommended for initial treatment in ART-naive pregnant women, there may be special circumstances in which ART-experienced women may need to continue or initiate ETR, NVP, MVC, and T-20 in order to maintain or achieve viral suppression. There are limited safety and efficacy data about the use of ETR, MVC, and T-20 in pregnancy. NVP is not recommended for ART-naive women because it has a greater potential for adverse events than other NNRTIs, complex lead-in dosing, and a low barrier to resistance; however, if a pregnant woman presents to care on a well-tolerated, NVP-containing regimen, it is likely that NVP will be safe and effective during pregnancy. See Table 4 and Nevirapine for more information.

[h] When using FDC tablets, refer to Table 8 and the drug sections in Appendix B for information about the dosing and safety of individual components of the FDC tablet during pregnancy.

[i] Testing for HLA-B*5701 identifies patients who are at risk of developing hypersensitivity reactions while taking ABC; testing should be performed and a patient should be documented as negative before initiating ABC.

[j] Available data about the use of TAF in pregnancy support continuing it in pregnant women who are virally suppressed, although data are insufficient to recommend it when initiating ART in pregnancy.

[k] Two-drug ARV regimens **are not recommended** for use in pregnancy.

The following drugs and drug combinations (that are not listed above) should not be used during pregnancy; if a woman becomes pregnant while taking any of these medications, she should switch to a recommended regimen: d4T, ddI, FPV, FPV/r, IDV, IDV/r, NFV, RTV (as the sole PI), SQV, SQV/r, TPV, TPV/r, or a three-NRTI ARV regimen (e.g., ABC/ZDV/3TC). See Archived Drugs in the Perinatal Guidelines and What Not to Use in the Adult and Adolescent Antiretroviral Guidelines for individual ARV drugs, ARV combinations, and ARV regimens that are not recommended or that should not be used in adults. Refer to the table above and Table 4 for ARV regimens that are recommended for use in pregnancy.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IBA =ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 6. Neonatal Antiretroviral Management According to Risk of HIV Infection in the Newborn

Drug selection and dosing considerations are related to the age and gestational age of the newborn. Consultation is available through the National Perinatal HIV Hotline (1-888-448-8765).

Level of Perinatal HIV Transmission Risk	Description	Neonatal ARV Management
Low Risk of Perinatal HIV Transmission	Mothers who received ART during pregnancy with sustained viral suppression (defined as a confirmed HIV RNA level < 50 copies/ml) near delivery and no concerns related to adherence	ZDV for 4 weeks
Higher Risk of Perinatal HIV Transmission[a,b]	Mothers who received neither antepartum nor intrapartum ARV drugs Mothers who received only intrapartum ARV drugs Mothers who received antepartum and intrapartum ARV drugs but who have detectable viral loads near delivery, particularly when delivery was vaginal Mothers with acute or primary HIV infection during pregnancy or breastfeeding (in which case, the mother **should discontinue breastfeeding**)[c]	Empiric HIV therapy using either ZDV, 3TC, and NVP (treatment dose) or ZDV, 3TC, and RAL administered from birth to age 6 weeks.[d] *or* Two-drug ARV prophylaxis (NICHD-HPTN 040/ PACTG 1043 regimen) with 6 weeks ZDV and three doses of NVP (prophylactic dose, with doses given within 48 hours of birth, 48 hours after first dose, and 96 hours after second dose)
Presumed Newborn HIV Exposure	Mothers with unconfirmed HIV status who have at least one positive HIV test at delivery or postpartum *or* Whose newborns have a positive HIV antibody test	ARV management as described above for newborns with a higher risk of perinatal HIV transmission Infant ARV drugs should be discontinued immediately if supplemental testing confirms that the mother does not have HIV

[a] See text for evidence that supports the use of empiric HIV therapy and a two-drug ARV prophylaxis regimen.

[b] See Intrapartum Care for guidance on indications for scheduled cesarean delivery and intrapartum IV ZDV to reduce the risk of perinatal HIV transmission for mothers with an elevated viral load at delivery.

[c] Most Panel members would opt to administer empiric HIV therapy to infants whose mothers had acute HIV during pregnancy because of the higher risk for *in utero* transmission. If acute HIV is diagnosed during breastfeeding, the mother should stop breastfeeding.

[d] The optimal duration of empiric HIV therapy in newborns at higher risk of perinatal HIV transmission is unknown. Some Panel members opt to discontinue NVP, RAL, and/or 3TC when a NAT performed shortly after birth returns negative, while others would continue empiric HIV therapy for infants at highest risk of HIV acquisition for 2 to 6 weeks. In all cases, ZDV should be continued for 6 weeks. It is recommended that providers consult with an expert in pediatric HIV infection to determine therapy duration based on case-specific risk factors and interim HIV NAT results.

[e] Most Panel members do not recommend delaying the initiation of ART pending results of the confirmatory HIV NAT, given the low likelihood of a false-positive HIV NAT.

Note: ARV drugs should be initiated as close to the time of birth as possible, preferably within 6 to 12 hours of delivery. See Table 7 for dosing specifics.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV =antiretroviral; IV = intravenous; NAT = nucleic acid test; NVP = nevirapine; the Panel = Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; RAL = raltegravir; ZDV = zidovudine

Table 7. Antiretroviral Dosing Recommendations for Newborns (page 1 of 3)

Newborns at Low Risk of Perinatal HIV Transmission	
Recommended Regimen	**Recommended Duration**
ZDV	ZDV administered for 4 weeks
Newborns at Higher Risk of Perinatal HIV Transmission	
Recommended Regimen	**Recommended Duration**
Empiric HIV therapy with ZDV plus 3TC plus NVP, *or*	ZDV administered for 6 weeks; 3TC and NVP administered for 2–6 weeks, up to 6 weeks of age[a]
Empiric HIV therapy with ZDV plus 3TC plus RAL, *or*	ZDV administered for 6 weeks; 3TC and RAL administered for 2–6 weeks, up to 6 weeks of age[a]
Two-drug ARV prophylaxis with ZDV and three doses of NVP (NICHD-HPTN 040/PACTG 1043 regimen)	ZDV administered for 6 weeks; three doses of NVP during the first week of life
Newborns with HIV Infection	
Recommended Regimen	**Recommended Duration[b]**
HIV therapy with ZDV plus 3TC plus NVP, *or*	Lifelong therapy. NVP can be replaced with LPV/r when infant reaches a postmenstrual age ≥42 weeks and a postnatal age ≥14 days; NVP can be replaced with RAL at any age.
HIV therapy with ZDV plus 3TC plus RAL	Lifelong therapy

<table>
<tr><th colspan="4">Indication</th></tr>
<tr><th>Drug</th><th>Low-Risk Prophylaxis</th><th>Higher-Risk Prophylaxis: Two-Drug Regimens</th><th>Higher-Risk Prophylaxis: Empiric and HIV Therapy</th></tr>
<tr><td rowspan="3">ZDV

Note: For newborns who are unable to tolerate oral agents, the IV dose is 75% of the oral dose while maintaining the same dosing interval.</td><td colspan="2">≥35 Weeks Gestation at Birth:
• ZDV 4 mg/kg per dose orally twice daily

Simplified Weight-Band Dosing for Newborns Aged ≥35 Weeks Gestation at Birth
<table><tr><th>Weight Band</th><th>Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</th></tr><tr><td>2 to <3 kg</td><td>1 mL</td></tr><tr><td>3 to <4 kg</td><td>1.5 mL</td></tr><tr><td>4 to <5 kg</td><td>2 mL</td></tr></table></td><td>≥35 Weeks Gestation at Birth
Birth to Age 4 Weeks:
• ZDV 4 mg/kg per dose orally twice daily
Age >4 Weeks:
• ZDV 12 mg/kg per dose orally twice daily

Simplified Weight-Band Dosing for Newborns Aged ≥35 Weeks Gestation from Birth to 4 Weeks
<table><tr><th>Weight Band</th><th>Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</th></tr><tr><td>2 to <3 kg</td><td>1 mL</td></tr><tr><td>3 to <4 kg</td><td>1.5 mL</td></tr><tr><td>4 to <5 kg</td><td>2 mL</td></tr></table></td></tr>
<tr><td colspan="2">≥30 to <35 Weeks Gestation at Birth
Birth to Age 2 Weeks:
• ZDV 2 mg/kg per dose orally twice daily
Age 2 Weeks to 4–6 Weeks:
• ZDV 3 mg/kg per dose orally twice daily</td><td>≥30 to <35 Weeks Gestation at Birth
Birth to Age 2 Weeks:
• ZDV 2 mg/kg per dose orally twice daily
Age 2 Weeks to 6–8 Weeks:
• ZDV 3 mg/kg per dose orally twice daily
Age >6 to 8 Weeks:
• ZDV 12 mg/kg per dose orally twice daily</td></tr>
<tr><td colspan="2"><30 Weeks Gestation at Birth
Birth to Age 4–6 Weeks:
• ZDV 2 mg/kg per dose orally twice daily</td><td><30 Weeks Gestation at Birth
Birth to Age 4 Weeks:
• ZDV 2 mg/kg per dose orally twice daily
Age 4 to 8–10 Weeks:
• ZDV 3 mg/kg per dose orally twice daily
Age >8 to 10 Weeks:
• ZDV 12 mg/kg per dose orally twice daily</td></tr>
</table>

Table 7. Antiretroviral Dosing Recommendations for Newborns (page 2 of 3)

<table>
<tr><th colspan="4">Indication</th></tr>
<tr><th>Drug</th><th>Low-Risk Prophylaxis</th><th>Higher-Risk Prophylaxis: Two-Drug Regimens</th><th>Higher-Risk Prophylaxis: Empiric and HIV Therapy</th></tr>
<tr><td>3TC</td><td>NRS</td><td>NRS</td><td>≥32 Weeks Gestation at Birth
Birth to Age 4 Weeks:
• 3TC 2 mg/kg per dose orally twice daily
Age >4 Weeks:
• 3TC 4 mg/kg per dose orally twice daily</td></tr>
<tr><td>NVP</td><td>NRS</td><td>≥32 Weeks Gestation at Birth:
• NVP in three doses, given within 48 hours of birth, 48 hours after the first dose, and 96 hours after the second dose
Birth Weight 1.5 to 2 kg:
• NVP 8 mg per dose orally. No calculation is required for this dose; <u>this is the actual dose, not a mg/kg dose</u>.
Birth Weight >2 kg:
• NVP 12 mg per dose orally. No calculation is required for this dose; <u>this is the actual dose, not a mg/kg dose</u>.</td><td>≥37 Weeks Gestation at Birth
Birth to Age 4 Weeks:
• NVP 6 mg/kg per dose orally twice daily[c]
Age >4 Weeks:
• NVP 200 mg/m^2 of BSA per dose orally twice daily
34 to <37 Weeks Gestation at Birth
Birth to Age 1 Week:
• NVP 4 mg/kg per dose orally twice daily
Age 1–4 Weeks:
• NVP 6 mg/kg per dose orally twice daily
Age >4 Weeks:
• NVP 200 mg/m^2 of BSA per dose orally twice daily
Note: NVP dose adjustment at 4 weeks of age is optional for empiric HIV therapy.</td></tr>
<tr><td>RAL
Note: If the mother has taken RAL 2–24 hours prior to delivery, the neonate's first dose of RAL should be delayed until 24–48 hours after birth; additional ARV drugs should be started as soon as possible.[7]</td><td>NRS</td><td>NRS</td><td>≥37 Weeks Gestation at Birth and Weighing ≥2 kg[d]
Birth to Age 6 Weeks
<table>
<tr><th>Body Weight</th><th>Volume (Dose) of RAL 10 mg/mL Suspension</th></tr>
<tr><td>Birth to 1 Week: Once Daily Dosing</td><td>Approximately 1.5 mg/kg per dose</td></tr>
<tr><td>2 to <3 kg</td><td>0.4 mL (4 mg) once daily</td></tr>
<tr><td>3 to <4 kg</td><td>0.5 mL (5 mg) once daily</td></tr>
<tr><td>4 to <5 kg</td><td>0.7 mL (7 mg) once daily</td></tr>
<tr><td>1 to 4 Weeks: Twice Daily Dosing</td><td>Approximately 3 mg/kg per dose</td></tr>
<tr><td>2 to <3 kg</td><td>0.8 mL (8 mg) twice daily</td></tr>
<tr><td>3 to <4 kg</td><td>1 mL (10 mg) twice daily</td></tr>
<tr><td>4 to <5 kg</td><td>1.5 mL (15 mg) twice daily</td></tr>
<tr><td>4 to 6 Weeks: Twice Daily Dosing</td><td>Approximately 6 mg/kg per dose</td></tr>
<tr><td>3 to <4 kg</td><td>2.5 mL (25 mg) twice daily</td></tr>
<tr><td>4 to <6 kg</td><td>3 mL (30 mg) twice daily</td></tr>
<tr><td>6 to <8 kg</td><td>4 mL (40 mg) twice daily</td></tr>
</table></td></tr>
</table>

[a] The optimal duration of empiric HIV therapy in newborns at higher risk of perinatal HIV transmission is unknown. Some Panel members opt to discontinue NVP, RAL, and/or 3TC when birth NAT returns negative, while others would continue empiric HIV therapy for infants at the highest risk of HIV acquisition for 2–6 weeks. In all cases in which the newborn is at higher risk of HIV acquisition, ZDV should be continued for 6 weeks. Consulting an expert in pediatric HIV is recommended when selecting a therapy duration based on case-specific risk factors and interim HIV NAT results.

[b] For ARV management after the newborn period, see the Pediatric Antiretroviral Guidelines.

Table 7. Antiretroviral Dosing Recommendations for Newborns (page 3 of 3)

[c] This dose is an investigational NVP treatment dose recommended by the Panel; the FDA has not approved a dose of NVP for infants aged <1 month.

[d] RAL dosing is increased at 1 and 4 weeks of age because metabolism by UGT1A1 is low at birth and increases rapidly during the next 4–6 weeks of life. No dosing information is available for preterm infants or infants weighing <2 kg at birth.

Key: 3TC = lamivudine; ARV =antiretroviral; BSA = body surface area; FDA = Food and Drug Administration; IV = intravenous; LPV/r = lopinavir/ritonavir; NAT = nucleic acid test; NRS = no recommendation specified; NVP = nevirapine; the Panel = the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; RAL = raltegravir; UGT = uridine diphosphate glucotransferase; ZDV = zidovudine

Appendix B: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy

Table 8. Antiretroviral Drug Use in Pregnant Women with HIV: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 1 of 18)

Note: When using FDCs, refer to other sections in Appendix B and Table 8 for information about the dosing and safety of individual drug components of the FDC during pregnancy.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
NRTIs NRTIs are recommended for use as part of combination regimens, usually including 2 NRTIs with either an NNRTI or 1 or more PIs. Use of single or dual NRTIs alone is not recommended for treatment of HIV infection. See text for discussion of potential maternal and infant mitochondrial toxicity.				
Abacavir (ABC) *Ziagen* (ABC/3TC) *Epzicom* (ABC/DTG/3TC) *Triumeq* (ABC/3TC/ZDV) *Trizivir* **Note:** Generic products are available for some formulations.	**ABC (Ziagen)**[d] *Tablet:* • 300 mg *Oral Solution:* • 20 mg/mL **ABC/3TC (Epzicom):**[d] • ABC 600 mg/3TC 300 mg tablet **ABC/DTG/3TC (Triumeq):** • ABC 600 mg/DTG 50 mg/3TC 300 mg tablet **ABC/3TC/ZDV (Trizivir):**[d] • ABC 300 mg/3TC 150 mg/ZDV 300 mg tablet	**Standard Adult Doses** *ABC (Ziagen):* • ABC 300 mg twice daily or ABC 600 mg once daily, without regard to food *ABC/3TC (Epzicom):* • One tablet once daily without regard to food *ABC/DTG/3TC (Triumeq):* • One tablet daily without regard to food *ABC/3TC/ZDV (Trizivir):* • One tablet twice daily without regard to food **Pregnancy** *PKs in Pregnancy:* • PKs not significantly altered in pregnancy. *Dosing in Pregnancy:* • No change in dose indicated. For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, ZDV, DTG).	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). HSRs occur in approximately 5% to 8% of nonpregnant individuals. A small percentage of reactions are fatal, and these fatal reactions are usually associated with re-challenge. Rate of reactions during pregnancy is unknown. Testing for HLA-B*5701 identifies patients at risk of reactions, and a patient's status **should be documented as negative** before initiating ABC. Patients should be educated regarding symptoms of HSR.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 2 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Emtricitabine (FTC) *Emtriva* (FTC/EFV/TDF) *Atripla* (FTC/BIC/TAF) *Biktarvy* (FTC/RPV/TDF) *Complera* (FTC/TAF) *Descovy* (FTC/EVG/c/TAF) *Genvoya* (FTC/RPV/TAF) *Odefsey* (FTC/EVG/c/TDF) *Stribild* (FTC/DRV/c/TAF) *Symtuza* (FTC/TDF) *Truvada* **Note:** Generic products are available for some formulations.	**FTC (Emtriva)** *Capsule:*[d] • 200 mg *Oral Solution:* • 10 mg/mL **FTC/EFV/TDF (Atripla):**[d] • FTC 200 mg/EFV 600 mg/TDF 300 mg tablet **FTC/BIC/TAF (Biktarvy):** • FTC 200 mg/BIC 50 mg/TAF 25 mg tablet **FTC/RPV/TDF (Complera):** • FTC 200 mg/RPV 25 mg/TDF 300 mg tablet **FTC/TAF (Descovy):** • FTC 200 mg/TAF 25 mg tablet **FTC/EVG/c/TAF (Genvoya):** • FTC 200 mg/EVG 150 mg/COBI 150 mg/TAF 10 mg tablet **FTC/RPV/TAF (Odefsey):** • FTC 200 mg/RPV 25 mg/TAF 25 mg tablet **FTC/EVG/c/TDF (Stribild):** • FTC 200 mg/EVG 150 mg/COBI 150 mg/TDF 300 mg tablet **FTC/DRV/c/TAF (Symtuza):** • FTC 200 mg/DRV 800 mg/COBI 150 mg/TAF 10 mg tablet **FTC/TDF (Truvada):**[d] • FTC 200 mg/TDF 300 mg tablet	**Standard Adult Doses** *FTC (Emtriva)* Capsule: • FTC 200 mg once daily without regard to food Oral Solution: • FTC 240 mg (24 mL) once daily without regard to food *FTC/EFV/TDF (Atripla):* • One tablet once daily at or before bedtime • Take on an empty stomach to reduce or mitigate side effects. *FTC/BIC/TAF (Biktarvy):* • One tablet once daily with or without food *FTC/RPV/TDF (Complera):* • One tablet once daily with food *FTC/TAF (Descovy):* • One tablet once daily with or without food *FTC/EVG/c/TAF (Genvoya):* • One tablet once daily with food *FTC/RPV/TAF (Odefsey):* • One tablet once daily with food *FTC/EVG/c/TDF (Stribild):* • One tablet once daily with food *FTC/DRV/c/TAF (Symtuza):* • One tablet once daily with food *FTC/TDF (Truvada):* • One tablet once daily without regard to food **Pregnancy** *PKs in Pregnancy:* • PKs of FTC are not significantly altered in pregnancy. *Dosing in Pregnancy:* • No change in dose indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., TDF, TAF, EFV, RPV, DRV, EVG, BIC, COBI).	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). If patient has HBV/HIV coinfection, it is possible that a HBV flare may occur if the drug is stopped; see Hepatitis B Virus/HIV Coinfection.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 3 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Lamivudine (3TC) *Epivir* (3TC/TDF) *Cimduo* (3TC/ZDV) *Combivir* (3TC/DOR/TDF) *Delstrigo* (3TC/DTG) *Dovato* (3TC/ABC) *Epzicom* (3TC/EFV/TDF) *Symfi* (3TC/EFV/TDF) *Symfi Lo* (3TC/TDF) *Temixys* (3TC/ABC/DTG) *Triumeq* (3TC/ABC/ZDV) *Trizivir* **Note:** Generic products are available for some formulations.	**3TC (Epivir)**[d] *Tablets:* • 150 mg • 300 mg *Oral Solution:* • 10 mg/mL **3TC/TDF (Cimduo):** • 3TC 300 mg/TDF 300 mg tablet **3TC/ZDV (Combivir):**[d] • 3TC 150 mg/ZDV 300 mg tablet **3TC/DOR/TDF (Delstrigo):** • 3TC 300 mg/DOR 100 mg/TDF 300 mg tablet **3TC/DTG (Dovato):** • 3TC 300 mg/DTG 50 mg tablet **3TC/ABC (Epzicom):**[d] • 3TC 300 mg/ABC 600 mg tablet **3TC/EFV/TDF (Symfi):** • 3TC 300 mg/EFV 600 mg/TDF 300 mg tablet **3TC/EFV/TDF (Symfi Lo):** • 3TC 300 mg/EFV 400 mg/TDF 300 mg tablet **3TC/TDF (Temixys):** • 3TC 300 mg/TDF 300 mg tablet **3TC/ABC/DTG (Triumeq):** • 3TC 300 mg/ABC 600 mg/DTG 50 mg tablet **3TC/ABC/ZDV (Trizivir):**[d] • 3TC 150 mg/ABC 300 mg/ZDV 300 mg tablet	**Standard Adult Doses** *3TC (Epivir):* • 3TC 150 mg twice daily or 300 mg once daily, without regard to food *3TC/TDF (Cimduo):* • One tablet once daily without regard to food *3TC/ZDV (Combivir):* • One tablet twice daily without regard to food *3TC/DOR/TDF (Delstrigo):* • One tablet once daily without regard to food *3TC/DTG (Dovato):* • One tablet once daily without regard to food *3TC/ABC (Epzicom):* • One tablet once daily without regard to food *3TC/EFV/TDF (Symfi or Symfi Lo):* • One tablet once daily on an empty stomach and preferably at bedtime *3TC/TDF (Temixys):* • One tablet once daily without regard to food *3TC/ABC/DTG (Triumeq):* • One tablet once daily without regard to food *3TC/ABC/ZDV (Trizivir):* • One tablet twice daily without regard to food **Pregnancy** *PKs in Pregnancy:* • PKs not significantly altered in pregnancy. *Dosing in Pregnancy:* • No change in dose indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., ABC, DOR, DTG, EFV, TDF, ZDV)	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). If patient has HBV/HIV coinfection, it is possible that an HBV flare may occur if the drug is stopped; see Hepatitis B Virus/HIV Coinfection. 3TC products that were developed specifically for treatment of HBV (e.g., Epivir-HBV) contain a lower dose of 3TC that **is not appropriate** for treatment of HIV.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 4 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Tenofovir Alafenamide (TAF) *Vemlidy* (TAF/BIC/FTC) *Biktarvy* (TAF/FTC) *Descovy* (TAF/EVG/c/FTC) *Genvoya* (TAF/FTC/RPV) *Odefsey* (TAF/DRV/c/FTC) *Symtuza*	**TAF (Vemlidy)** *Tablet:* • 25 mg **TAF/BIC/FTC (Biktarvy):** • TAF 25 mg/BIC 50 mg/FTC 200 mg tablet **TAF/FTC (Descovy):** • TAF 25 mg/FTC 200 mg tablet **TAF/EVG/c/FTC (Genvoya):** • TAF 10 mg/EVG 150 mg/COBI 150 mg/FTC 200 mg tablet **TAF/FTC/RPV (Odefsey):** • TAF 25 mg/FTC 200 mg/RPV 25 mg tablet **TAF/DRV/c/FTC (Symtuza):** • TAF 10 mg/DRV 800 mg/COBI 150 mg/FTC 200 mg tablet	**Standard Adult Doses** *TAF (Vemlidy):* • One tablet once daily with food *TAF/BIC/FTC (Biktarvy):* • One tablet once daily with or without food *TAF/FTC (Descovy):* • One tablet once daily with or without food • Same dose (TAF 25 mg) can be used with or without PK enhancers. *TAF/EVG/c/FTC (Genvoya):* • One tablet once daily with food *TAF/FTC/RPV (Odefsey):* • One tablet once daily with food *TAF/DRV/c/FTC (Symtuza):* • One tablet once daily with food **Pregnancy** *PKs in Pregnancy:* • Plasma PKs not significantly altered in pregnancy. *Dosing in Pregnancy:* • No change in dose indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., BIC, COBI, DRV, EVG, FTC, RPV).	Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats. Renal function should be monitored because of the potential for renal toxicity.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 5 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Tenofovir Disoproxil Fumarate (TDF) *Viread* (TDF/EFV/FTC) *Atripla* (TDF/3TC) *Cimduo* (TDF/FTC/RPV) *Complera* (TDF/DOR/3TC) *Delstrigo* (TDF/EVG/c/FTC *Stribild* (TDF/EFV/3TC) *Symfi* (TDF/EFV/3TC) *Symfi Lo* (TDF/3TC) *Temixys* (TDF/FTC) *Truvada* **Note:** Generic products are available for some formulations.	**TDF (Viread)** *Tablet:*[d] • 300 mg *Powder:* • 40 mg/1 g oral powder **TDF/EFV/FTC (Atripla):** • TDF 300 mg/EFV 600 mg/FTC 200 mg tablet **TDF/3TC (Cimduo):** • TDF 300 mg/3TC 300 mg tablet **TDF/FTC/RPV (Complera):** • TDF 300 mg/FTC 200 mg/RPV 25 mg tablet **TDF/DOR/3TC (Delstrigo):** • TDF 300 mg/DOR 100 mg/3TC 300 mg tablet **TDF/EVG/c/FTC (Stribild):** • TDF 300 mg/EVG 150 mg/COBI 150 mg/FTC 200 mg tablet **TDF/EFV/3TC (Symfi):** • TDF 300 mg/EFV 600 mg/3TC 300 mg tablet **TDF/EFV/3TC (Symfi Lo):** • TDF 300 mg/EFV 400 mg/3TC 300 mg tablet **TDF/3TC (Temixys):** • TDF 300 mg/3TC 300 mg tablet **TDF/FTC (Truvada):** • TDF 300 mg/FTC 200 mg tablet	**Standard Adult Doses** *TDF (Viread)* Tablet: • TDF 300 mg once daily without regard to food Powder: • TDF 8 mg/kg daily (up to a maximum of TDF 300 mg). Take with food. *TDF/EFV/FTC (Atripla):* • One tablet once daily at or before bedtime. Take on an empty stomach to reduce side effects. *TDF/3TC (Cimduo):* • One tablet once daily without regard to food *TDF/FTC/RPV (Complera):* • One tablet once daily with food *TDF/DOR/3TC (Delstrigo):* • One tablet once daily without regard to food *TDF/EVG/c/FTC (Stribild):* • One tablet once daily with food *TDF/EFV/3TC (Symfi or Symfi Lo):* • One tablet once daily on an empty stomach and preferably at bedtime *TDF/3TC (Temixys):* • One tablet once daily without regard to food *TDF/FTC (Truvada):* • One tablet once daily without regard to food **Pregnancy** *PKs in Pregnancy:* • AUC is lower in third trimester than postpartum, but trough levels are adequate. *Dosing in Pregnancy:* • No change in dose is indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, COBI, DOR, EFV, EVG, FTC, RPV)	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Studies in monkeys (at doses approximately 2-fold higher than those for human therapeutic use) show decreased fetal growth and reduction in fetal bone porosity within 2 months of starting maternal therapy. Human studies demonstrate no consistent link to low birth weight, but data are conflicting about potential effects on growth outcomes later in infancy. If patient has HBV/HIV coinfection, it is possible that an HBV flare may occur if TDF is stopped; see Hepatitis B Virus/HIV Coinfection. Renal function should be monitored because of potential for renal toxicity.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 6 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Zidovudine (ZDV) *Retrovir* (ZDV/3TC) *Combivir* (ZDV/ABC/3TC) *Trizivir* **Note:** Generic products are available for all formulations.	**ZDV (Retrovir)** *Capsule:* • 100 mg *Tablet:* • 300 mg *Oral Solution:* • 10 mg/mL *IV Solution:* • 10 mg/mL **ZDV/3TC (Combivir):** • ZDV 300 mg/3TC 150 mg tablet **ZDV/ABC/3TC (Trizivir):** • ZDV 300 mg/ABC 300 mg/3TC 150 mg tablet	**Standard Adult Doses** *ZDV (Retrovir):* • ZDV 300 mg twice daily or ZDV 200 mg three times a day without regard to food • Patients in active labor should receive ZDV 2 mg/kg IV as a loading dose, followed by ZDV 1 mg/kg/hour continuous infusion from beginning of active labor until delivery. *ZDV/3TC (Combivir):* • One tablet twice daily without regard to food *ZDV/ABC/3TC (Trizivir):* • One tablet twice daily without regard to food **Pregnancy** *PKs in Pregnancy:* • PKs not significantly altered in pregnancy. *Dosing in Pregnancy:* • No change in dose indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., ABC, 3TC)	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects).	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 7 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
NNRTI NNRTIs are recommended for use in combination regimens with 2 NRTI drugs. Hypersensitivity reactions, including hepatic toxicity and rash, more common in women; unclear if increased in pregnancy.				
Doravirine (DOR) *Pifeltro* (DOR/3TC/TDF) *Delstrigo*	**DOR (Pifeltro):** • 100 mg tablet **DOR/3TC/TDF (Delstrigo):** • DOR 100 mg/ 3TC 300 mg/ TDF 300 mg tablet	**Standard Adult Doses** *DOR (Pifeltro):* • DOR 100 mg once daily with or without food *DOR/3TC/TDF (Delstrigo):* • One tablet once daily with or without food **Pregnancy** *PKs in Pregnancy:* • No PK studies in human pregnancy. *Dosing in Pregnancy:* • Insufficient data to make dosing recommendations. For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, TDF)	No data are available on the placental transfer of DOR in humans, but animal studies suggest that DOR crosses the placenta. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.	December 24, 2019
Efavirenz (EFV) *Sustiva* (EFV/FTC/TDF) *Atripla* (EFV/3TC/TDF) *Symfi* (EFV/3TC/TDF) *Symfi Lo* **Note:** Generic products are available for some formulations.	**EFV (Sustiva)**[d] *Capsules:* • 50 mg • 200 mg *Tablet:* • 600 mg **EFV/FTC/TDF (Atripla):** • EFV 600 mg/FTC 200 mg/TDF 300 mg tablet **EFV/3TC/TDF (Symfi):** • EFV 600 mg/3TC 300 mg/TDF 300 mg tablet **EFV/3TC/TDF (Symfi Lo):** • EFV 400 mg/3TC 300 mg/TDF 300 mg tablet	**Standard Adult Doses** *EFV (Sustiva):* • EFV 600 mg once daily at or before bedtime • Take on an empty stomach to reduce side effects. *EFV/FTC/TDF (Atripla):* • One tablet once daily at or before bedtime • Take on an empty stomach to reduce side effects. *EFV/3TC/TDF (Symfi or Symfi Lo):* • One tablet once daily on an empty stomach and preferably at bedtime **Pregnancy** *PKs in Pregnancy:* • AUC is decreased during the third trimester compared with postpartum, but nearly all third-trimester participants exceeded target exposure.	Moderate placental transfer to fetus.[b] The FDA advises women to avoid becoming pregnant while taking EFV and advises health care providers to avoid administration during the first trimester of pregnancy, as fetal harm may occur. However, the data on more than 7,900 periconception EFV exposures from Botswana rules out a ≥3-fold increased risk of NTDs. As a result, the current Perinatal Guidelines do not restrict the use of EFV in pregnant women or in women who are planning to become pregnant. This is consistent with both the British HIV Association and WHO guidelines for use of ARV drugs in pregnancy. EFV should be continued in pregnant women who are on a virally suppressive, EFV-based regimen, because ARV drug changes during pregnancy may be associated with loss of viral control and an increased risk of perinatal transmission (see Pregnant Women Living with HIV Who are Currently Receiving Antiretroviral Therapy).	January 17, 2020

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 8 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Efavirenz, continued		*Dosing in Pregnancy:* • No change in dose is indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, FTC, TDF)		
Etravirine (ETR) *Intelence*	**Tablets:** • 25 mg • 100 mg • 200 mg For patients who are unable to swallow tablets whole, the tablets may be dispersed in a glass of water.	**Standard Adult Dose:** • ETR 200 mg twice daily with food **Pregnancy** *PKs in Pregnancy:* • PK data in pregnancy suggest 1.2-fold to 1.6-fold increases in ETR exposure during pregnancy. *Dosing in Pregnancy:* • No change in dose indicated.	Placental transfer varies; it is usually in the moderate to high categories, ranging from 0.19–4.25.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.	December 24, 2019
Nevirapine (NVP) *Viramune* *Viramune XR* **Note:** Generic products are available for some formulations.	**NVP (Viramune)** *Tablet:* • 200 mg[d] *Oral Suspension:* • 50 mg/5 mL[d] **Viramune XR** *Tablets:* • 100 mg • 400 mg[d]	**Standard Adult Doses:** • NVP 200 mg once daily (using Viramune immediate release) for a 14-day lead-in period; thereafter, NVP 200 mg twice daily or 400 mg (using Viramune XR tablet) once daily, without regard to food. • Repeat lead-in period if therapy is discontinued for >7 days. • In patients who develop mild-to-moderate rash without constitutional symptoms during the lead-in period, continue lead-in dosing until rash resolves, but administer for ≤28 days total. **Pregnancy** *PKs in Pregnancy:* • PKs of immediate-release tablets not significantly altered in pregnancy. • No data available on extended-release formulations in pregnancy. *Dosing in Pregnancy:* • No change in dose indicated.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects and 2-fold increase in cardiovascular and genitourinary defects). There is an increased risk of symptomatic liver toxicity when first initiating therapy in women with CD4 counts ≥250/mm^3. Liver toxicity is often associated with a rash and can be fatal. Pregnancy does not appear to increase this risk. NVP should be initiated in pregnant women with CD4 counts ≥250 cells/mm^3 only if benefit clearly outweighs risk. There is a potential increased risk of life-threatening hepatotoxicity in women with high CD4 counts. Elevated transaminase levels at baseline may increase the risk of NVP toxicity. Women who become pregnant while taking NVP-containing regimens and who are tolerating their regimens well can continue taking those regimens, regardless of their CD4 counts.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 9 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Rilpivirine (RPV) *Edurant* (RPV/FTC/TDF) *Complera* (RPV/DTG) *Juluca* (RPV/FTC/TAF) *Odefsey*	**RPV (Edurant)** *Tablets:* • 25 mg **RPV/FTC/TDF (Complera):** • RPV 25 mg/FTC 200 mg/TDF 300 mg tablet **RPV/DTG (Juluca):** • RPV 25 mg/DTG 50 mg tablet **RPV/FTC/TAF (Odefsey):** • RPV 25 mg/FTC 200 mg/TAF 25 mg tablet	**Standard Adult Doses** *RPV (Edurant):* • RPV 25 mg once daily with food *RPV/FTC/TDF (Complera):* • One tablet once daily with food *RPV/DTG (Juluca):* • One tablet once daily with food *RPV/FTC/TAF (Odefsey):* • One tablet once daily with food **Pregnancy** *PKs in Pregnancy:* • RPV PKs are highly variable during pregnancy. RPV AUC and trough concentration are 20% to 50% lower in pregnancy than postpartum. While most pregnant women exceeded target exposure, those with detectable viral loads had lower RPV troughs. *Dosing in Pregnancy:* • While RPV plasma concentration is reduced during pregnancy, higher-than-standard doses have not been studied, and there is not enough data available to recommend a dosing change during pregnancy. Pregnant women receiving standard dosing should have their viral loads monitored more frequently than women who are not receiving RPV. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., DTG, FTC, TAF, TDF).	Moderate to high placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects). Two-drug regimens (e.g., the RPV/DTG FDC) **are not recommended** for use in pregnancy.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 10 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
PIs PIs block the activity of the protease enzyme, which is required to assemble new HIV viral particles that are capable of infecting new cells.				
Atazanavir (ATV) *Reyataz* **Note:** Generic products are available for some formulations. **Note:** ATV must be combined with low-dose RTV boosting in pregnancy. (ATV/c) *Evotaz*	**ATV (Reyataz)** *Capsules:* • 100 mg (generic product only) • 150 mg[d] • 200 mg[d] • 300 mg[d] *Oral Powder:* • 50 mg packet **ATV/c (Evotaz):** • ATV 300 mg/ COBI 150 mg tablet	**Standard Adult Doses** *In ARV-Naive Patients without RTV Boosting:* • ATV 400 mg once daily with food; ATV without RTV boosting **is not recommended** when used with TDF, H2-receptor antagonists, PPIs, or during pregnancy. *In ARV-Naive Patients with RTV Boosting:* • ATV 300 mg plus RTV 100 mg once daily with food • When combined with EFV in ARV-naive patients: ATV 400 mg plus RTV 100 mg once daily with food *In ARV-Experienced Patients:* • ATV 300 mg plus RTV 100 mg once daily with food • **Do not use** with PPIs or EFV *In ARV-Experienced Patients Who Are Receiving an H2-Receptor Antagonist:* • ATV 300 mg plus RTV 100 mg once daily with food *In ARV-Experienced Patients Who Are Receiving an H2-Receptor Antagonist and TDF:* • ATV 400 mg plus RTV 100 mg once daily with food *Powder Formulation:* • Oral powder is taken with RTV once daily with food at the same recommended adult dose as the capsules. *ATV/c (Evotaz):* • One tablet once daily with food **Pregnancy** *PKs in Pregnancy* ATV (Reyataz): • ATV concentrations are reduced during pregnancy, and they are further reduced when ATV is given concomitantly with TDF or an H2-receptor antagonist. ATV/c (Evotaz): • Use of ATV/c **is not recommended** during pregnancy, because ATV trough concentrations are 80% to 85% lower than the ATV concentrations seen in nonpregnant adults.	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Must be given with RTV boosting in pregnancy. Effect of *in utero* ATV exposure on infant indirect bilirubin levels is unclear. Nonpathologic elevations of neonatal bilirub have been observed in some, but not all, clinical trials to date. Oral powder (but **not** capsules) contains phenylalanine, which can be harmful to patients with phenylketonuria. Use of ATV/c **is not recommended** during pregnancy. See Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 4, and Table 5 for discussions about avoiding the use of ATV/c during pregnancy.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 11 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Atazanavir, continued		*Dosing in Pregnancy* ATV (Reyataz): • Use of unboosted ATV **is not recommended** during pregnancy. • Use of ATV **is not recommended** for ARV-experienced pregnant women who are taking TDF and an H2-receptor antagonist. • Use of an increased dose (ATV 400 mg plus RTV 100 mg once daily with food) during the second and third trimesters results in plasma ATV concentrations equivalent to those seen in nonpregnant adults receiving standard dosing. Although some experts recommend increased ATV dosing in all women during the second and third trimesters, the package insert recommends increased ATV dosing only for ARV-experienced pregnant women in the second and third trimesters who are also receiving either TDF or an H2-receptor antagonist. ATV/c (Evotaz): • Insufficient data to make dosing recommendation in pregnancy (see COBI). For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., COBI).		
Darunavir (DRV) *Prezista* **Note:** Must be combined with low-dose RTV or COBI boosting. (DRV/c) *Prezcobix* (DRV/c/FTC/TAF) *Symtuza*	**DRV (Prezista)** *Tablet:* • 75 mg • 150 mg • 600 mg • 800 mg *Oral Suspension:* • 100 mg/mL **DRV/c (Prezcobix):** • DRV/c 800 mg/150 mg tablet **DRV/c/FTC/TAF (Symtuza):** • DRV 800 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg tablet	**Standard Adult Doses** *ARV-Naive Patients:* • DRV 800 mg plus RTV 100 mg once daily with food • DRV 800 mg plus COBI 150 mg once daily with food *ARV-Experienced Patients* If Patient Has No DRV Resistance Mutations: • DRV 800 mg plus RTV 100 mg once daily with food • DRV 800 mg plus COBI 150 mg once daily with food If Any DRV Resistance Mutations Are Present: • DRV 600 mg plus RTV 100 mg twice daily with food *DRV/c (Prezcobix):* • One tablet once daily with food *DRV/c/FTC/TAF (Symtuza):* • One tablet once daily with food **Pregnancy** *PKs in Pregnancy:* • Decreased exposure in pregnancy with use of DRV/r.	Low placental transfer to fetus.[b] No evidence of teratogenicity in mice, rats, or rabbits. No evidence of human teratogenicity. Must be boosted with low-dose RTV. The Panel **does not recommend** once-daily dosing with DRV/r during pregnancy or the use of DRV/c during pregnancy. If a DRV/c regimen is continued during pregnancy, viral load should be monitored frequently.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 12 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Darunavir, continued		*Dosing in Pregnancy:* • The Panel **does not recommend** once-daily dosing with DRV/r during pregnancy or the use of DRV/c during pregnancy. • Twice-daily DRV/r dosing (DRV 600 mg plus RTV 100 mg with food) is recommended for all pregnant women. • Increased twice-daily DRV dose (DRV 800 mg plus RTV 100 mg with food) during pregnancy does not result in an increase in DRV exposure and **is not recommended**. For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., COBI, FTC, TAF)		
Lopinavir/ Ritonavir (LPV/r) *Kaletra*	**LPV/r (Kaletra)** *Tablets:* • LPV/r 200 mg/50 mg • LPV/r 100 mg/25 mg *Oral Solution:* • Each 5 mL contains LPV/r 400 mg/100 mg	**Standard Adult Doses:** • LPV/r 400 mg/100 mg twice daily, *or* • LPV/r 800 mg/200 mg once daily *Tablets:* • Take without regard to food. *Oral Solution:* • Take with food. *With EFV or NVP in PI-Naive or PI-Experienced Patients:* • LPV/r 500 mg/125 mg tablets twice daily without regard to meals (use a combination of two LPV/r 200 mg/50 mg tablets and one LPV/r 100 mg/25 mg tablet), *or* • LPV/r 520 mg/130 mg oral solution (6.5 mL) twice daily with food **Pregnancy** *PKs in Pregnancy:* • With twice-daily dosing, LPV exposure is reduced in pregnant women who receive standard adult doses; increasing the dose by 50% results in exposure equivalent to that seen in nonpregnant adults receiving standard doses. • No PK data are available for once-daily dosing in pregnancy. *Dosing in Pregnancy:* • Once-daily dosing **is not recommended** during pregnancy. • Some experts recommend that an increased dose (i.e., LPV/r 600 mg/150 mg twice daily without regard to meals or LPV/r 500 mg/125 mg twice daily without regard to meals) should be used in the second and third trimesters, especially in PI-experienced pregnant women and women who start treatment during pregnancy with a baseline viral load >50 copies/mL. • When standard dosing is used, monitor virologic response and, if possible, LPV drug levels.	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Oral solution contains 42% alcohol and 15% propylene glycol and **is not recommended** for use in pregnancy. Once-daily LPV/r dosing **is not recommended** during pregnancy.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 13 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Entry Inhibitors Entry and attachment inhibitors block viral binding or fusion of HIV to host cells.				
Ibalizumab (IBA) *Trogarzo*	**IBA (Trogarzo):** • Solution for IV infusion is available in single-dose vials	**Standard Adult Dose:** • IBA 2,000-mg loading dose, followed by IBA 800-mg maintenance doses administered every 2 weeks **Pregnancy** *PKs in Pregnancy:* • No PK studies in human pregnancy. *Dosing in Pregnancy:* • Insufficient data to make dosing recommendations.	No data available, but placental transfer of IBA, a monoclonal antibody, is possible. Insufficient data to assess for teratogenicity in humans.	December 24, 2019
Maraviroc (MVC) *Selzentry*	**MVC (Selzentry)** *Tablets:* • 150 mg • 300 mg	**Standard Adult Doses:** • MVC 300 mg twice daily with or without food • MVC should only be used for patients with CCR5-tropic virus (and no X4-tropic virus). *Dose Adjustments:* • Increase to MVC 600 mg twice daily when used with the potent CYP3A inducers EFV, ETR, and rifampin. • Decrease to MVC 150 mg twice daily when used with CYP3A inhibitors, which includes all PIs except TPV/r and itraconazole. **Pregnancy** *PKs in Pregnancy:* • A PK study in human pregnancy demonstrated a 20% to 30% overall decrease in MVC AUC, but C_{trough} exceeded the recommended minimum concentration of 50 ng/mL. *Dosing in Pregnancy:* • Adjusting the standard adult MVC dose for concomitant use with ARV drugs seems appropriate.	Moderate placental transfer to fetus.[b] No evidence of teratogenicity in rats or rabbits; insufficient data to assess for teratogenicity in humans.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 14 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
INSTIs INSTIs block integrase, the viral enzyme that catalyzes the two-step process that inserts HIV DNA into the genome of the host cell.				
Bictegravir/ Emtricitabine/ Tenofovir Alafenamide (BIC/FTC/TAF) *Biktarvy* **Note:** BIC is only available as part of an FDC tablet.	**BIC/FTC/TAF (Biktarvy):** • BIC 50 mg/FTC 200 mg/TAF 25 mg tablet	**Standard Adult Dose:** • One tablet once daily with or without food **Pregnancy** *PKs in Pregnancy:* • No PK studies in human pregnancy. *Dosing in Pregnancy:* • Insufficient data to make dosing recommendations. For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., FTC, TAF).	No data are available on placental transfer of BIC. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. BIC can be taken with food at the same time as any preparation containing iron or calcium, including prenatal vitamins, but should not be administered within 2 hours of these preparations when taken on an empty stomach. BIC can be taken at least 2 hours before or 6 hours after antacids containing aluminum or magnesium.	December 24, 2019
Dolutegravir (DTG) *Tivicay* (DTG/3TC) *Dovato* (DTG/RPV) *Juluca* (DTG/ABC/3TC) *Triumeq*	**DTG (Tivicay):** • DTG 50 mg tablet **DTG/3TC (Dovato):** • DTG 50 mg/3TC 300 mg tablet **DTG/RPV (Juluca):** • DTG 50 mg/ RPV 25 mg tablet **DTG/ABC/3TC (Triumeq):** • DTG 50 mg/ ABC 600 mg/3TC 300 mg tablet	**Standard Adult Doses** *In ARV-Naive or ARV-Experienced (but INSTI-Naive) Patients* DTG (Tivicay): • One tablet once daily, without regard to food DTG/3TC (Dovato): • One tablet once daily, without regard to food DTG/RPV (Juluca): • One tablet once daily with food DTG/ABC/3TC (Triumeq): • One tablet once daily, without regard to food *In ARV-Naive or ARV-Experienced (but INSTI-Naive) Patients Who Are Also Receiving EFV, FPV/r, TPV/r, or Rifampin* DTG (Tivicay): • One tablet twice daily, without regard to food *In INSTI-Experienced Patients* DTG (Tivicay): • One tablet twice daily, without regard to food **Pregnancy** *PKs in Pregnancy:* • AUC may be decreased during the third trimester compared with postpartum, but exposures during pregnancy are well above those needed to inhibit viral replication.	High placental transfer to fetus.[b] No evidence of teratogenicity in rats or rabbits. In pregnancy surveillance data from Botswana, there was a slightly increased risk of NTDs in infants born to women who initiated DTG prior to pregnancy and who were receiving it at the time of conception. DTG may be used as part of a *Preferred* regimen in all pregnant women at all gestational ages and as part of an *Alternative* regimen in women who are trying to conceive. Clinicians should discuss the risks and benefits of DTG use with the patient. For more information, see Updated Guidance About the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy. To maximize DTG absorption, doses should not be administered within 2 hours of ingesting any preparation that contains minerals such as iron or calcium, including prenatal vitamins.	December 12, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 15 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Dolutegravir, continued		*Dosing in Pregnancy:* • No change in dose indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., ABC, 3TC, RPV).		
Elvitegravir (EVG) **Note:** As of October 2017, the single-drug formulation of EVG (Vitekta) is no longer available. (EVG/c/FTC/TAF) *Genvoya* (EVG/c/FTC/TDF) *Stribild*	**EVG/c/FTC/TAF (Genvoya):** • EVG 150 mg/ COBI 150 mg/ FTC 200 mg/ TAF 10 mg tablet **EVG/c/FTC/TDF (Stribild):** • EVG 150 mg/ COBI 150 mg/ FTC 200 mg/ TDF 300 mg tablet	**Standard Adult Dose** *Genvoya and Stribild:* • One tablet once daily with food **Pregnancy** *PKs in Pregnancy:* • PK studies in women who received EVG/c demonstrated significant reduction in EVG plasma exposure during pregnancy. *Dosing in Pregnancy:* • EVG plasma concentrations are reduced with use of standard adult doses during pregnancy; however, higher-than-standard doses of EVG have not been studied. Insufficient data are available to recommend a dose for use in pregnancy. For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., COBI, FTC, TAF).	Evidence of high placental transfer of EVG and low transfer of COBI.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. EVG/c **is not recommended** for use in pregnancy. For women who become pregnant while taking EVG/c, consider switching to a more effective, recommended regimen. If a woman continues taking a regimen that contains EVG/c, doses should be administered with a meal and should not be administered within 2 hours of ingesting any preparation that contains minerals such as iron or calcium, including prenatal vitamins.	December 24, 2019
Raltegravir (RAL) *Isentress* *Isentress HD*	**RAL (Isentress)** *Film-Coated Tablets:* • 400 mg *Chewable Tablets:* • 25 mg • 100 mg **RAL (Isentress HD)** *Film-Coated Tablets:* • 600 mg	**Standard Adult Doses** *In Patients Who Are Not Receiving Rifampin:* • RAL 400-mg, film-coated tablets twice daily without regard to food • Two RAL 600-mg, film-coated tablets (1,200 mg) once daily without regard to food for ARV-naive patients or patients who are already virologically suppressed on an initial regimen of RAL 400 mg twice daily • Chewable tablets and oral suspension doses **are not interchangeable** with either film-coated tablets or each other. *In Patients Who Are Receiving Rifampin:* • Two RAL 400-mg, film-coated tablets (800 mg) twice daily without regard to food **Pregnancy** *PKs in Pregnancy:* • Decreased drug concentrations in third trimester are not of sufficient magnitude to warrant a change in dosing.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). There is a case report of markedly elevated liver transaminases with RAL use in late pregnancy. Severe, potentially life-threatening, and fatal skin and HSRs have been reported in nonpregnant adults. RAL chewable tablets contain phenylalanine. To maximize RAL absorption, doses should not be administered within 2 hours of ingestion of any preparation containing minerals such as iron or calcium, including prenatal vitamins.	January 17, 2020

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 16 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Integrase Inhibitors, continued				
Raltegravir, continued		*Dosing in Pregnancy:* • No change in dose is indicated. • Once-daily dosing (i.e., two RAL 600-mg, film-coated tablets) **should not be used** in pregnant women until more information is available.		
Pharmacoenhancers Pharmacoenhancers reduce the metabolism of antiretroviral drugs and prolong their presence in plasma, allowing for more convenient dosing regimens.				
Cobicistat (COBI) *Tybost* (ATV/c) *Evotaz* (EVG/c/FTC/TAF) *Genvoya* (DRV/c) *Prezcobix* (EVG/c/FTC/TDF) *Stribild* (DRV/c/FTC/TAF) *Symtuza*	**COBI (Tybost)** *Tablet:* • COBI 150 mg **ATV/c (Evotaz):** • ATV 300 mg/COBI 50 mg tablet **EVG/c/FTC/TAF (Genvoya):** • EVG 150 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg tablet **DRV/c (Prezcobix):** • DRV 800 mg/COBI 150 mg tablet **EVG/c/FTC/TDF (Stribild):** • EVG 150 mg/COBI 150 mg/FTC 200 mg/TDF 300 mg tablet **DRV/c/FTC/TAF (Symtuza):** • DRV 800 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg tablet	**Standard Adult Doses** *COBI (Tybost):* • When used as an alternative PK booster with ATV or DRV, the dose is one tablet once daily with food *ATV/c (Evotaz):* • One tablet once daily with food *EVG/c/FTC/TAF (Genvoya):* • One tablet once daily with food *DRV/c (Prezcobix):* • One tablet once daily with food *EVG/c/FTC/TDF (Stribild):* • One tablet once daily with food *DRV/c/FTC/TAF (Symtuza):* • One tablet once daily with food **Pregnancy** *PKs in Pregnancy:* • Based on limited data, COBI exposure and its pharmaco-enhancing effect on ATV, DRV, and EVG are markedly reduced in pregnancy. • When coadministered with COBI, TAF exposure is not significantly different between pregnancy and the postpartum period. *Dosing in Pregnancy:* • While COBI exposure is markedly reduced during pregnancy, higher-than-standard doses have not been studied. The Panel recommends RTV as the preferred pharmaco-enhancer for PIs and INSTIs during pregnancy until more data are available on COBI activity during pregnancy. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., FTC, TAF, TDF, ATV, DRV, EVG).	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects). Use of COBI-boosted ATV, DRV, or EVG **is not recommended** in pregnancy.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 17 of 18)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Ritonavir (RTV) *Norvir* (LPV/r) *Kaletra*	**RTV (Norvir)** *Capsules:* • RTV 100 mg *Tablets:* • RTV 100 mg *Oral Solution:* • RTV 80 mg/mL *Powder:* • RTV 100 mg/sachet **LPV/r (Kaletra)** *Tablets:* • LPV/r 200 mg/50 mg • LPV/r 100 mg/25 mg *Oral Solution:* • Each 5 mL contains LPV/r 400 mg/100 mg	**Standard Adult Dose of RTV (Norvir) When Used as PK Booster for Other PIs:** • RTV 100–400 mg per day in one or two divided doses (refer to other PI sections for specific dosing recommendations) *Tablet:* • Take with food *Capsule or Oral Solution:* • To improve tolerability, take with food if possible **Standard Adult Doses of LPV/r (Kaletra):** • LPV/r 400 mg/100 mg twice daily, *or* • LPV/r 800 mg/200 mg once daily *Tablets:* • Take without regard to food. *Oral Solution:* • Take with food. *With EFV or NVP in PI-Naive or PI-Experienced Patients:* • LPV/r 500 mg/125 mg tablets twice daily without regard to meals (use a combination of two LPV/r 200 mg/50 mg tablets and one LPV/r 100 mg/25 mg tablet), *or* • LPV/r 520 mg/130 mg oral solution (6.5 mL) twice daily with food **Pregnancy** *PKs in Pregnancy:* • Lower RTV levels are seen during pregnancy than during postpartum, which may reduce the pharmaco-enhancing effect of RTV in pregnancy. *RTV Dosing in Pregnancy:* • No dose adjustment necessary when RTV is used as booster. *LPV/r Dosing in Pregnancy:* • Once-daily dosing **is not recommended** during pregnancy. • Some experts recommend that an increased dose (i.e., LPV/r 600 mg/150 mg twice daily without regard to meals or LPV/r 500 mg/125 mg twice daily without regard to meals) should be used in the second and third trimesters, especially in PI-experienced pregnant women and women who start treatment during pregnancy with a baseline viral load >50 copies/mL. • When standard dosing is used, monitor virologic response and, if possible, LPV drug levels. For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., LPV/r).	Low placental transfer to fetus.[b] No evidence of increased risk of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). RTV should only be used as low-dose booster for other PIs. RTV oral solution contains 43% alcohol and therefore **is not recommended** for use during pregnancy, because there is no known safe level of alcohol exposure during pregnancy. LPV/r oral solution contains 42% alcohol and 15% propylene glycol and **is not recommended** for use in pregnancy. Once-daily LPV/r dosing **is not recommended** during pregnancy.	December 24, 2019

Table 8. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 18 of 18)

[a] Individual ARV drug dosages may need to be adjusted in patients with renal or hepatic insufficiency (for details, see the Adult and Adolescent Guidelines, Appendix B, Table 10).

[b] Placental transfer categories are determined by mean or median cord blood/maternal delivery plasma drug ratio:

High: >0.6 **Moderate:** 0.3–0.6 **Low:** <0.3

[c] Only indicated for use in chronic HBV virus infection in adults.

[d] Generic product available

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CD4 = CD4 T lymphocyte; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis b virus; HSR = hypersensitivity reaction; IBA =ibalizumab; INSTI = integrase strand transfer inhibitor; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; WHO = World Health Organization; ZDV = zidovudine

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 1 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
PACTG 076; United States, France;[1] Formula feeding	ZDV vs. placebo	Long (from 14 weeks) IV IP	Long (6 weeks); infant only	Perinatal transmission at 18 months was 8.3% in ZDV arm vs. 25.5% in placebo arm (68% efficacy).
CDC Short-Course ZDV Trial; Thailand;[12] Formula feeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	None	Perinatal transmission at 6 months was 9.4% in ZDV arm vs. 18.9% in placebo arm (50% efficacy).
DITRAME (ANRS 049a) Trial; Ivory Coast, Burkina Faso;[11,39] Breastfeeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	Short (1 week); mother only	Perinatal transmission at 6 months was 18.0% in ZDV arm vs. 27.5% in placebo arm (38% efficacy). Perinatal transmission at 15 months was 21.5% in ZDV arm vs. 30.6% in placebo arm (30% efficacy). Perinatal transmission was 22.5% in ZDV arm vs. 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy).
CDC Short-Course ZDV Trial; Ivory Coast;[10,11] Breastfeeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	None	Perinatal transmission at 3 months was 16.5% in ZDV arm vs. 26.1% in placebo arm (37% efficacy). Perinatal transmission was 22.5% in ZDV arm vs. 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy).
PETRA Trial; South Africa, Tanzania, Uganda;[5] Breastfeeding and formula feeding	AP/IP/PP ZDV plus 3TC vs. IP/PP ZDV plus 3TC vs. IP-only ZDV plus 3TC vs. Placebo	Short (from 36 weeks) Oral IP	Short (1 week); mother and infant	Perinatal transmission at 6 weeks was 5.7% for AP/IP/PP ZDV plus 3TC, 8.9% for IP/PP ZDV plus 3TC, 14.2% for IP-only ZDV plus 3TC, and 15.3% for placebo (efficacy compared with placebo: 63%, 42%, and 0%, respectively). Perinatal transmission at 18 months was 14.9% for AP/IP/PP ZDV plus 3TC, 18.1% for IP/PP ZDV plus 3TC, 20.0% for IP-only ZDV plus 3TC, and 22.2% for placebo (efficacy compared with placebo: 34%, 18%, and 0%, respectively).

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 2 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
HIVNET 012 Trial; Uganda;[4] Breastfeeding	SD NVP vs. ZDV	No AP ARV drugs Oral IP: • SD NVP vs. oral ZDV	SD NVP within 72 hours of birth; infant only vs. ZDV for 1 week; infant only	Perinatal transmission at 6–8 weeks was 11.8% in NVP arm vs. 20.0% in ZDV arm (42% efficacy) and 15.7% in NVP arm vs. 25.8% in ZDV arm at 18 months (41% efficacy).
SAINT Trial; South Africa;[6] Breastfeeding and formula feeding	SD NVP vs. ZDV plus 3TC	No AP ARV drugs Oral IP: • SD NVP vs. ZDV plus 3TC	SD NVP within 48 hours of birth; mother and infant vs. ZDV plus 3TC for 1 week; mother and infant	Perinatal transmission at 8 weeks was 12.3% in SD NVP arm vs. 9.3% in ZDV plus 3TC arm (difference not statistically significant, $P = 0.11$).
PHPT-1; Thailand;[13] Formula feeding	4 ZDV regimens with different durations of AP and infant PP administration; no placebo	Long (from 28 weeks) or short (from 36 weeks) Oral IP	Long (6 weeks) or short (3 days); infant only	Perinatal transmission rate was 10.5% in the short-short arm. This arm was stopped at interim analysis. Perinatal transmission at 6 months was 6.5% in long-long arm vs. 4.7% in long-short arm and 8.6% in short-long arm (no statistical difference). *In utero* transmission was significantly higher with short vs. long maternal therapy regimens (5.1% vs. 1.6%).
PACTG 316 Trial; Bahamas, Belgium, Brazil, France, Germany, Italy, Spain, Sweden, Switzerland, United Kingdom, United States;[21] Formula feeding	SD NVP vs. placebo among women already receiving ZDV alone (23%) or ZDV plus other ARV drugs (77% combination therapy)	Nonstudy ARV regimen Oral IP: • Placebo vs. SD NVP plus IV ZDV	Placebo vs. SD NVP within 72 hours of birth plus nonstudy ARV drugs (ZDV); infant only	77% of women received dual- or triple-combination ARV regimens during pregnancy. Trial stopped early because of very low perinatal transmission in both arms: 1.4% in SD NVP arm vs. 1.6% in placebo arm (53% of perinatal transmission was *in utero*).
PHPT-2; Thailand;[40] Formula feeding	ZDV alone vs. ZDV plus maternal and infant SD NVP vs. ZDV plus maternal SD NVP	ZDV from 28 weeks Oral IP: • ZDV alone, *or* • ZDV plus SD NVP	ZDV for 1 week with or without SD NVP; infant only	ZDV-alone arm was stopped because the rate of perinatal transmission was higher in this arm than in the ZDV/NVP arm (6.3% vs. 1.1%, respectively). In arms in which the mother received SD NVP, the perinatal transmission rate did not differ significantly whether the infant received SD NVP or not (2.0% vs. 2.8%, respectively).
DITRAME Plus (ANRS 1201.0) Trial; Ivory Coast;[15] Breastfeeding and formula feeding	Open label, ZDV plus SD NVP	ZDV from 36 weeks Oral IP: • ZDV plus SD NVP	SD NVP plus ZDV for 1 week; infant only	Perinatal transmission at 6 weeks was 6.5% (95% CI, 3.9% to 9.1%); perinatal transmission for historical control group receiving short ZDV (98% of whom were breastfed) was 12.8%.
DITRAME Plus (ANRS 1201.1) Trial; Ivory Coast;[15] Breastfeeding and formula feeding	Open label, ZDV plus 3TC plus SD NVP	ZDV plus 3TC from 32 weeks (stopped at 3 days PP) Oral IP: • ZDV plus 3TC plus SD NVP	SD NVP plus ZDV for 1 week; infant only	Perinatal transmission at 6 weeks was 4.7% (95% CI, 2.4% to 7.0%); perinatal transmission for historical control group receiving short ZDV (98% of whom were breastfed) was 12.8%.

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 3 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
NVAZ Trial; Malawi;[7] Breastfeeding	Neonatal SD NVP vs. SD NVP plus ZDV	No AP or IP ARV drugs	SD NVP with or without ZDV for 1 week; infant only	Perinatal transmission at 6–8 weeks was 15.3% in SD NVP plus ZDV arm vs. 20.9% in SD NVP-only arm. Perinatal transmission rates at 6–8 weeks among infants without HIV at birth were 7.7% and 12.1%, respectively (36% efficacy).
Postnatal NVP plus ZDV Trial; Malawi;[8] Breastfeeding	Neonatal SD NVP vs. SD NVP plus ZDV	No AP ARV Oral IP: • SD NVP	SD NVP with or without ZDV for 1 week; infant only	Perinatal transmission at 6–8 weeks was 16.3% in NVP plus ZDV arm vs. 14.1% in SD NVP-only arm (difference not statistically significant). Perinatal transmission rates at 6–8 weeks among infants without HIV at birth were 6.5% and 16.9%, respectively.
Post-Exposure Infant Prophylaxis; South Africa;[9] Breastfeeding and formula feeding	Neonatal SD NVP vs. ZDV for 6 weeks	No AP or IP ARV drugs	SD NVP vs. ZDV for 6 weeks	For formula-fed infants only, perinatal transmission at 6 weeks was 14.3% in SD NVP arm vs. 14.1% in ZDV arm (not significant, $P = 0.30$). For breastfed infants only, perinatal transmission was 12.2% in SD NVP arm vs. 19.6% in ZDV arm ($P = 0.03$).
Mashi; Botswana;[41,42] Breastfeeding and formula feeding	Initial: • Short-course ZDV with/without maternal and infant SD NVP and with/without breastfeeding Revised: • Short-course ZDV plus infant SD NVP with/without maternal SD NVP and with/without breastfeeding; women with CD4 counts <200 cells/mm^3 received combination therapy.	First Randomization: • ZDV from 34 weeks Oral IP: • ZDV plus either SD NVP or placebo	Second Randomization: • Breastfeeding plus ZDV (infant) 6 months plus SD NVP; infant only, vs. • Formula feeding plus ZDV (infant) 4 weeks plus SD NVP; infant only	Initial Design: • In formula-feeding arm, perinatal transmission at 1 month was 2.4% in maternal and infant SD NVP arm vs. 8.3% in placebo arm ($P = 0.05$). • In breastfeeding plus infant ZDV arm, perinatal transmission at 1 month was 8.4% in SD NVP arm vs. 4.1% in placebo arm (difference not statistically significant). Revised Design: • Perinatal transmission at 1 month was 4.3% in maternal plus infant SD NVP arm vs. 3.7% in maternal placebo plus infant SD NVP arm (no significant difference; no interaction with mode of infant feeding). Perinatal transmission at 7 months was 9.1% in breastfeeding plus ZDV arm vs. 5.6% in formula-feeding arm; mortality at 7 months was 4.9% in breastfeeding plus ZDV arm vs. 9.3% in formula-feeding arm; HIV-free survival at 18 months was 15.6% in the breastfeeding plus ZDV arm vs. 14.2% in the formula-feeding arm.
SWEN; Uganda, Ethiopia, India;[24] Breastfeeding	SD NVP vs. NVP for 6 weeks	No AP ARV drugs Oral IP: • SD NVP	Infant SD NVP vs. NVP for 6 weeks	Postnatal Infection in Infants Without HIV at Birth: • Perinatal transmission at 6 weeks was 5.3% in SD NVP arm vs. 2.5% in extended NVP arm (risk ratio 0.54, $P = 0.009$). • Perinatal transmission at 6 months was 9.0% in SD NVP arm vs. 6.9% in extended NVP arm (risk ratio 0.80, $P = 0.16$). HIV-free survival was significantly lower in extended NVP arm at both 6 weeks and 6 months of age.

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 4 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
PEPI-Malawi Trial; Malawi;[23] Breastfeeding	SD NVP plus ZDV for 1 week (control) vs. 2 extended infant regimens (NVP or NVP/ZDV) for 14 weeks	No AP ARV drugs Oral IP: • SD NVP (if mother presents in time)	Infant SD NVP plus ZDV for 1 week (control) vs. Control plus NVP for 14 weeks vs. Control plus NVP/ZDV for 14 weeks	Postnatal Infection in Infants Without HIV at Birth: • Perinatal transmission at 6 weeks was 5.1% in control arm vs. 1.7% in extended NVP arm (67% efficacy) and 1.6% in extended NVP/ZDV arm (69% efficacy). • Perinatal transmission at 9 months was 10.6% in control arm vs. 5.2% in extended NVP arm (51% efficacy) and 6.4% in extended NVP/ZDV arm (40% efficacy). No significant difference in perinatal transmission between the extended prophylaxis arms; however, more hematologic toxicity with NVP/ZDV.
MITRA; Tanzania;[26] Breastfeeding	Infant 3TC for 6 months (observational)	ZDV/3TC from 36 weeks through labor	Maternal ZDV/3TC for 1 week; infant 3TC for 6 months	Perinatal transmission at 6 months was 4.9% (postnatal perinatal transmission between 6 weeks and 6 months was 1.2%).
Kisumu Breastfeeding Study; Kenya;[29] Breastfeeding	Maternal triple-drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4 count >250 cells/mm^3) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4 count >250 cells/mm^3) for 6 months, infant SD NVP	Perinatal transmission at 6 months was 5.0% (postnatal perinatal transmission between 7 days and 6 months was 2.6%).
MITRA-PLUS; Tanzania;[25] Breastfeeding	Maternal triple-drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4 count >200 cells/mm^3) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4 count >200 cells/mm^3) for 6 months, infant ZDV/3TC for 1 week	Perinatal transmission at 6 months was 5.0% (postnatal perinatal transmission between 6 weeks and 6 months was 0.9%), not significantly different from 6-month infant prophylaxis in MITRA.
Kesho Bora; Multi-African;[28] Breastfeeding primarily	AP ZDV/SD NVP with no postnatal prophylaxis vs. Maternal triple-drug prophylaxis in women with CD4 counts 200–500 cells/mm^3	Arm 1: • ZDV/3TC/LPV/r Arm 2: • ZDV plus SD NVP From 28 weeks through labor	Arm 1: • Maternal ZDV/3TC/LPV/r for 6 months, infant SD NVP plus ZDV for 1 week Arm 2: • Maternal ZDV/3TC for 1 week (no further postnatal prophylaxis), infant SD NVP plus ZDV for 1 week (no further postnatal prophylaxis)	Perinatal transmission at birth was 1.8% with maternal triple-drug prophylaxis (Arm 1) vs. 2.5% with ZDV/SD NVP (Arm 2), not significantly different. In women with CD4 counts 350–500 cells/mm^3, perinatal transmission at birth was 1.7% in both arms. Perinatal transmission at 12 months was 5.4% with maternal triple-drug prophylaxis (Arm 1) vs. 9.5% with ZDV/SD NVP (with no further postnatal prophylaxis after 1 week) (Arm 2) (P = 0.029).
Mma Bana; Botswana;[2] Breastfeeding	Compared 2 maternal triple-drug prophylaxis regimens in women with CD4 counts >200 cells/mm^3	Arm 1: • ZDV/3TC/ABC Arm 2: • ZDV/3TC/LPV/r From 26 weeks through labor	Arm 1: • Maternal ZDV/3TC/ABC for 6 months, infant SD NVP plus ZDV for 4 weeks Arm 2: • Maternal ZDV/3TC/LPV/r for 6 months, infant SD NVP plus ZDV for 4 weeks	Perinatal transmission at 6 months overall was 1.3%: 2.1% in ZDV/3TC/ABC Arm 1 vs. 0.4% in ZDV/3TC/LPV/r Arm 2 (P = 0.53).

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 5 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
BAN; Malawi;[27,43] **Breastfeeding**	Postpartum maternal triple-drug prophylaxis vs. infant NVP in women with CD4 counts ≥250 cells/mm^3	No AP drugs IP Regimens *Arm 1 (Control):* • ZDV/3TC plus SD NVP *Arm 2:* • ZDV/3TC plus SD NVP *Arm 3:* • ZDV/3TC plus SD NVP	Arm 1 (Control): • Maternal ZDV/3TC for 1 week; infant SD NVP plus ZDV/3TC for 1 week Arm 2: • Control as above, then maternal ZDV/3TC/LPV/r for 6 months Arm 3: • Control as above, then infant NVP for 6 months	Postnatal Infection in Infants Without HIV at 2 Weeks: • Perinatal transmission at 28 weeks was 5.7% in control Arm 1, 2.9% in maternal triple-drug prophylaxis Arm 2 (P = 0.009 vs. control), and 1.7% in infant NVP Arm 3 (P < 0.001 vs. control). • Perinatal transmission at 48 weeks was 7.0% in control Arm 1, 4.0% in maternal triple-drug prophylaxis Arm 2 (P = 0.0273 vs. control), and 4% in infant NVP Arm 3 (P = 0.0027 vs. control). No significant difference between maternal triple-drug prophylaxis (Arm 2) and infant NVP (Arm 3) (P = 0.12 at 28 weeks and P = 0.426 at 48 weeks).
HPTN 046; South Africa, Tanzania, Uganda, Zimbabwe;[38,44] **Breastfeeding**	Postpartum prophylaxis to prevent breast milk transmission of HIV with 6 weeks of infant NVP vs. 6 months of infant NVP	AP drugs allowed if required for maternal health	All infants received daily NVP from birth through age 6 weeks. Arm 1: • Daily infant NVP from 6 weeks through 6 months Arm 2: • Daily infant placebo from 6 weeks through 6 months	In infants without HIV at age 6 weeks, the 6-month infant HIV infection rate was 1.1% (0.3% to 1.8%) in the extended NVP arm vs. 2.4% (1.3% to 3.6%) in the placebo arm (P = 0.048). 18-month postnatal infection rates were 2.2% (1.1% to 3.3%) in the extended NVP arm vs. 3.1% (1.9% to 4.4%) in the placebo arm (P = 0.28). HIV infection and mortality rates did not differ between arms at any age through 18 months. At infant randomization at age 6 weeks, 29% of mothers in each arm were receiving a triple-drug ARV regimen for the treatment of HIV. For mothers receiving triple-drug ARV regimens at the time of randomization, in infants without HIV at age 6 weeks, the 6-month infant HIV infection rate was 0.2% and not statistically different from the rates seen in the extended NVP arm (0.5%) and placebo arm (0%). For mothers with CD4 counts >350 cells/mm^3 who were not receiving triple-drug ARV regimens, in infants without HIV at age 6 weeks, the 6-month infant HIV infection rate was 0.7% (0% to 1.5%) in the extended NVP arm vs. 2.8% (1.3% to 4.4%) in the placebo arm (P = 0.014).

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 6 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
NICHD-HPTN 040/ PACTG 1043 Trial; Brazil, Argentina, South Africa, United States;[45] Formula feeding	Infant prophylaxis with 6 weeks of ZDV vs. 6 weeks of infant ZDV plus 3 doses of NVP in first week of life vs. 6 weeks of infant ZDV plus 2 weeks 3TC/NFV	No AP drugs If mother presented early enough, IV ZDV during labor through delivery	Arm 1 (Control): • Infant ZDV for 6 weeks Arm 2: • Control as above plus NVP, with first dose within 48 hours of birth, second dose 48 hours later, and third dose 96 hours after second dose Arm 3: • Control as above, plus 3TC and NFV from birth through age 2 weeks	IP HIV transmission among infants with negative HIV test at birth: 4.8% (3.2% to 7.1%) with ZDV (Arm 1) vs. 2.2% (1.2% to 3.9%) with ZDV plus NVP (Arm 2) (*P* = 0.046 compared with Arm 1) vs. 2.4% (1.4% to 4.3%) with ZDV plus 3TC/NFV (Arm 3) (*P* = 0.046 compared with Arm 1). Overall HIV transmission rates, including *in utero* infection: 11.0% (8.7% to 14.0%) with ZDV (Arm 1) vs. 7.1% (5.2% to 9.6%) with ZDV plus NVP (Arm 2) (*P* = 0.035 compared with Arm 1) vs. 7.4% (5.4% to 9.9%) with ZDV plus 3TC/NFV (Arm 3) (*P* = 0.035 compared with Arm 1). Grade 3 or 4 neutropenia more frequent in ZDV/3TC/NFV Arm 3 (70 infants) than in ZDV-alone Arm 1 (33 infants) or ZDV/NVP Arm 2 (32 infants) (*P* < 0.001).
ANRS 12174 Trial; Burkina Faso, South Africa, Uganda, Zambia;[30,31] Breastfeeding	Compared 2 infant ARV prophylaxis regimens during breastfeeding; infants tested PCR-negative at birth and were born to mothers with CD4 counts >350 cells/mm^3	As per standard of care	Arm 1: • Daily infant LPV/r from 1 week through 50 weeks of age Arm 2: • Daily infant 3TC from 1 week through 50 weeks of age	Postnatal Infection in Infants Without HIV at Birth: • Postnatal transmission at age 50 weeks was 1.4% (0.70–2.76) in Arm 1 vs. 1.5% (0.80–2.91) in Arm 2 (*P* = 0.83). • HIV-free survival was 96.5% (84.6–97.7) in Arm 1 vs. 96.3% (94.4–97.5) in Arm 2 (*P* = 0.85).
PROMOTE; Uganda;[46] Breastfeeding	Compared 2 triple-ARV regimens; no CD4 restriction	Arm 1: • ZDV/3TC/LPV/r Arm 2: • ZDV/3TC/EFV • ARVs started at 12–28 weeks' gestation and continued through labor	Randomized regimen continued postpartum through 1 year of breastfeeding	HIV-free survival was 92.9% in the LPV/r arm vs. 97.2% in the EFV arm (*P* = 0.10). Only 2 of 374 liveborn infants acquired infection, both in the LPV/r arm.
PROMISE; India, Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe;[18] Breastfeeding and formula feeding (antepartum component)	Compared ZDV prophylaxis and 2 ART regimens during pregnancy among women at >14 weeks' gestation and with CD4 counts ≥350 cells/mm^3	Arm 1: • ZDV during pregnancy plus SD NVP plus TDF plus FTC at delivery Arm 2: • ZDV plus 3TC plus LPV/r Arm 3: • TDF plus FTC plus LPV/r	Arm 1: • TDF/FTC tail continued for 6–14 days postpartum Arms 2 and 3: • ART regimen continued for 6–14 days postpartum Infants received once-daily NVP for 6 weeks.	Infant HIV Infection Rates by Age 14 Days *Arm 1:* • 1.8% (25/1,386) *Arm 2:* • 0.5% (7/1,385) *Arm 3:* • 0.6% (2/325) Combined ART arms vs. ZDV arm difference in perinatal transmission risk: -1.3% (95% CI, -2.1% to -0.4%)

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 7 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
PROMISE; India, Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe;[18] Breastfeeding (postpartum component)	Compared infant NVP and maternal ART during breastfeeding among infants born to women with CD4 counts ≥350 cells/mm^3	This was a postpartum study. intervention only. Eligible women included women enrolled in PROMISE antepartum (see above) and women who received no ARV drugs during pregnancy.	Arm 1: • Mothers received TDF plus FTC plus LPV/r Arm 2: • Once-daily infant NVP Regimens were continued until 42 days after last breastmilk exposure or age 18 months, whichever came first.	Infant Infection Rates: *Arm 1:* • 0.57% (7/1,219) *Arm 2:* • 0.58% (7/1,211) Rates of Infant HIV-1–Free Survival at 24 Months *Arm 1:* • 97.1% *Arm 2:* • 97.7%

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; AP = antepartum; ARV = antiretroviral; ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; CI = confidence interval; EFV = efavirenz; FTC = emtricitabine; IP = intrapartum; IV = intravenous; LPV/r = lopinavir/ritonavir; NFV = nelfinavir; NVP = nevirapine; PCR = polymerase chain reaction; PP = postpartum; SD = single-dose; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine